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Substance Use from Adolescence to Young Adulthood: Contributions from Social Experiences and Neural Response to Rewards and Social Situations

By

SARAH JANE MCMILLAN
DISSERTATION

Submitted in partial satisfaction of the requirements for the degree of

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DEDICATION

To my uncle, Thomas Steven McMillan (1955 – 2023). Thank you for loaning me books from the Library of Tom, encouraging me to become a lifelong scholar, and inspiring my love of travel. I'll always remember your excitement upon hearing that I was moving to California to pursue this PhD. Repose en paix, mon cher oncle.

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Pursuing this PhD allowed me to explore a lifelong curiosity about people and the world around us, and this journey would not have been possible without the support of so many people. I've had the privilege to work with brilliant scientists, meet new friends, and learn not only about the developing brain, but also myself; and all with the love and support of family and friends.

Thank you to my team of mentors for investing their time in me. To Amanda Guyer, who took a chance on a student with no neuroimaging experience. Your thoughtful approach and thorough feedback have made me a better scholar. I often ask myself, "What is the guiding question?" in your voice, reminding me of the bigger contexts of our work. To Paul Hastings, for your kindness, passion, and encouragement to stick with ideas when I didn't believe in myself. And for sharing recipes for persimmons when I had a ton and no idea what to do with them.

To Johnna Swartz, who first trained me on operating an MRI machine, and helped me become organized in my data analysis and writing processes. To Maciel Hernández, for inspiring me to contextualize my work within participants' communities, connecting me with resources to strengthen skills, and sharing career opportunities. To Beth Cauffman, who made an impact on me years ago at a conference professional development lunch, and collaborated on an exciting project (even if it was a victim of COVID-19). To Kim Berardi, for your endless compassion and cheerleading. I would also like to extend my gratitude to the professors I have worked with as a teaching assistant, including Joseph Anistranski, Meng Huo, Adrienne Nishina, and Siwei Liu.

I am so fortunate to have been a part of the TEEN Lab, with labmates past and present, including Leehyun Yoon, Angelica Carranza, Rajpreet Chahal, and Joe Venticinque. Thank you, Joe, for making graduate school fun (i.e., making the impossible possible). On the day we first met during your campus visit, I felt like we clicked; and I really hoped you would join the lab. I

would also like to thank the HERD Lab, including Elisa Ugarte, Lisa Johnson, and Lindsey Partington. Elisa, you'll always be #AcademicBae along with the rest of our PhD cohort, Xiaoya Zhang and Jennie Bullen. And Elisa's kitties, Luchín and Yoyi. A huge thank you to Amanda Mangurten, the best peer mentor – and Helen Fann and Kristina Sayler, for our coven meetings. I also extend my gratitude to my past teachers, including Elda Hall-Yee, Kyle Eckman, and Jennifer Hough-Duda. Kyle, thank you for convincing me that I needed to go to college.

Thank you, Jason Grotuss, for your unconditional love and support that sustained me through the stresses of graduate school. You always made sure that I ate, took walks, and at least attempted to sleep, even when it meant physically pulling my chair away from the desk when it was long past the time of quitting. Earning this PhD would not have been possible without you.

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Kathryn, my soul sister ever since the third grade, thank you for your love and support. I'm grateful for you organizing game nights, spoiling me during visits, and being the kind of friend who can pick up right where we left off after not seeing each other for months. Thank you to my dear friends Bridgett, Lisa, Xenia, Ann, Evan, and Candy, for sticking by my side even when I never answered messages. (I promise to work on that, now that my PhD is not an excuse.)

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ABSTRACT

Substance use during adolescence is a major public health concern, given the deleterious effects excessive use can have on brain development and social functioning into young adulthood. Past work has characterized how substance use is associated with neural response to monetary reward, and self-reported social support and stress; but less is known about associations among substance use, social experiences, and neural responses to social stimuli. Given that substance use often occurs in social contexts, there is a need to identify how neural response to social stimuli predicts substance use, especially in diverse samples such as Latinx populations, who face both greater vulnerability to high-risk use and greater risk of experiencing ethnic-racial discrimination. This dissertation examined how substance use across adolescence and young adulthood was associated with neural response to monetary reward, social inclusion, and social exclusion, as well as self-reported experiences of social support and social stress, in Mexican-origin individuals. Study 1 investigated bidirectional relations among adolescent neural response to social and monetary rewards and self-reported substance use from adolescence (age 16) to young adulthood (age 21), testing both cross-lagged effects and change scores to comprehensively capture change in neural function and substance use. Study 2 assessed the interplay of neural response to a social stressor, self-reported substance use, and self-reported experiences of social support and social stress from late childhood (age 10) to young adulthood (age 21). Further, Study 2 tested whether adolescent neural response to social exclusion and self-reported resistance to peer influence mediated links among substance use, social support (perceived support from family and friends, endorsed familism values), social stress (victimization by peers, ethnic-racial discrimination), and young-adult indicators of social functioning (social support, prosocial behaviors, romantic relationship quality). Study 1 results

showed that neural activity to social reward in mid-adolescence predicted steeper increases in substance use by young adulthood, and that change in neural response to monetary reward was linked to change in substance use. Study 2 findings showed that early adolescent familism and social support predicted less substance use during young adulthood, partially mediated by adolescents' response to social exclusion in the subgenual anterior cingulate cortex. Early experiences of ethnic-racial discrimination were associated with higher substance use, but not mediated by neural activity during social exclusion. Conversely, reporting more years of substance use by adolescence predicted less prosocial behavior and less support from family and friends during young adulthood; but neural activity to social exclusion and self-reported resistance to peer influence did not explain these associations. Taken together, these studies highlight the importance of how the developing brain processes socially-rewarding situations, non-socially rewarding situations, and socially-stressful situations. Neural sensitivity to social rewards and socially-stressful situations may be unique biomarkers that identify adolescents at high risk for excessive substance use. Understanding socio-neural predictors and consequences of substance use is key to prevention and intervention efforts designed for adolescents and young adults. Additionally, prevention and intervention programs that focus on individual behaviors without considering social context may be less effective, and especially so for certain adolescents who are highly sensitive biologically to peer behaviors and influences. Addressing substance use during adolescence can reduce the development of substance use disorders in adulthood, and its associated personal and financial costs to society.

CHAPTER ONE

GENERAL INTRODUCTION

The use of substances (e.g., alcohol, cannabis, and tobacco) is a significant public health concern that typically escalates from adolescence to young adulthood (Miech et al., 2024). Potential consequences of excessive substance use include cognitive deficits, social problems, and incarceration (King et al., 2006; Squeglia & Cservenka, 2017; Thoma et al., 2011). For young adults aged 20 to 24 years old, 14% of deaths result from substance-induced causes, such as unintentional overdose (Centers for Disease Control and Prevention, 2021). During the adolescent years, substance use ranges from short-lived experimentation to high-risk patterns. Monitoring the Future (MTF), a national survey of middle- and high-school students in the U.S., reported that 60% of adolescents have used alcohol and 50% have tried an illicit drug by the end of high school (Miech et al., 2024). Although some experimentation is unlikely to have long-term consequences, substance use disorders (SUDs) are estimated to affect 12% of adolescents (Center for Behavioral Health Statistics & Quality, 2020). Earlier use predicts worse outcomes; for example, adolescents who began drinking before age 15 have four- to six-times the rate of lifetime dependence than those who waited until 21 to drink. Substance use can negatively impact brain structure and function (Debenham et al., 2021; Lees et al., 2021), as well as social functioning (Clay & Parker, 2018; Sinha, 2008). These problems are compounded by health disparities in the risks and consequences of substance use among racial and ethnic minorities.

Substance use is more prevalent among, and has an earlier onset in, Latinx adolescents compared to White adolescents on average (Atherton et al., 2016; Trent et al., 2023). Results from MTF have indicated that Hispanic/Latino adolescents are twice as likely to report binge drinking (i.e., consuming 5 or more drinks within a short period of time) than White adolescents,

and three times more likely than African-American adolescents (Miech et al., 2024). Additionally, McCauley et al. (2024) revealed greater use of tobacco and cannabis through e-cigarette devices among Latinx adolescents and young adults versus their White and African-American counterparts. These ethnic/racial differences may exist because Latinx individuals face unique social stressors, such as discrimination based on race and/or ethnicity (Vitoroulis & Georgiades, 2017); however, they may also benefit from cultural assets such as familism, a traditional Latinx value focused on family closeness and obligation (Lardier et al., 2018). These unique risk and protective factors may further shape and be shaped by the brain's processing of salient information, yet most developmental neuroscience research has relied upon White, educated, industrialized, rich, and democratic (WEIRD) samples (Burns et al., 2019; Chiao & Cheon, 2010; Qu et al., 2021); and although more studies have begun recruiting more ethno-racially diverse samples, knowledge gaps remain. Another limitation is that social factors remain under-studied, despite the relevance of adolescents' social contexts and social experiences for their engagement in substance use (Beard et al., 2022b).

Although cognitive and motivational processes are important, substance use does not occur in a vacuum. Most youth begin experimenting because someone offers them substances in social situations (Dishion & Tipsord, 2011; Teunissen et al., 2012). Adolescence is characterized by more time spent with peers (Ashbourne & Daly, 2012), and perceptions of peers' behaviors and attitudes about substance use are consistently implicated in adolescents' use (Brechwald & Prinstein, 2011; Gallegos et al., 2021). Indeed, MTF has suggested that forces in the social environment may influence adolescents' attitudes and beliefs about substances, as well as their use of them (Miech et al., 2024). Friends' use is strongly associated with individual use, likely reflecting three causal patterns: (1) an adolescent with friends who use a substance will be more

likely to try it, (2) an adolescent who is already using a substance will be more likely to introduce their friends to it, and (3) substance-using adolescents are more likely to make friends with other youths who also use substances, while substance-avoiding adolescents are more likely to befriend substance-avoiding peers. Thus, the behavioral literature has implied that peer influence on substance use involves a combination of selection and socialization effects.

Beyond direct influence, adolescence is also marked by a strong sensitivity to social evaluation, and potential social threats (Guyer & Jarcho, 2018; Nelson et al., 2016). Given the social contexts in which substance use often begins, understanding how the brain responds to social experiences would provide much-needed information about the development of substance use and SUDs. Existing work on social influences and adolescent brain function has focused on risk-taking more generally, rather than substance use specifically. Studies that assess substance use in adults often compare individuals with and without SUDs, or they do not distinguish between young adults and older adults. Thus, there is a need to examine social processes in the brain (e.g., receiving social rewards, experiencing social stressors) during adolescence and young adulthood as they relate to concurrent and future substance use.

In my systematic review of 28 fMRI studies assessing alcohol and cannabis use in adolescents and young adults (Beard et al., 2022b), we identified that only three studies had examined social reward, and five had examined social stress including my pre-dissertation research project (Beard, et al., 2022a). Although a small number of other studies have been published since then, these gaps in the literature remain. Based on this review, my dissertation was designed to address these gaps through two studies that examined how social reward and social stress influence substance use. In Study 1, I tested how neural response to social and non-social rewards was associated with substance use from mid-adolescence to early young

adulthood. In Study 2, I investigated the interplay of substance use, neural response to a social stressor, and experiences of social support and social stress from late childhood to young adulthood. This dissertation builds upon previous findings from neuroimaging research documenting neural response to different types of rewards, behavioral work about social functioning, and developmental theory proposed to explain onset and increase in substance use during adolescence.

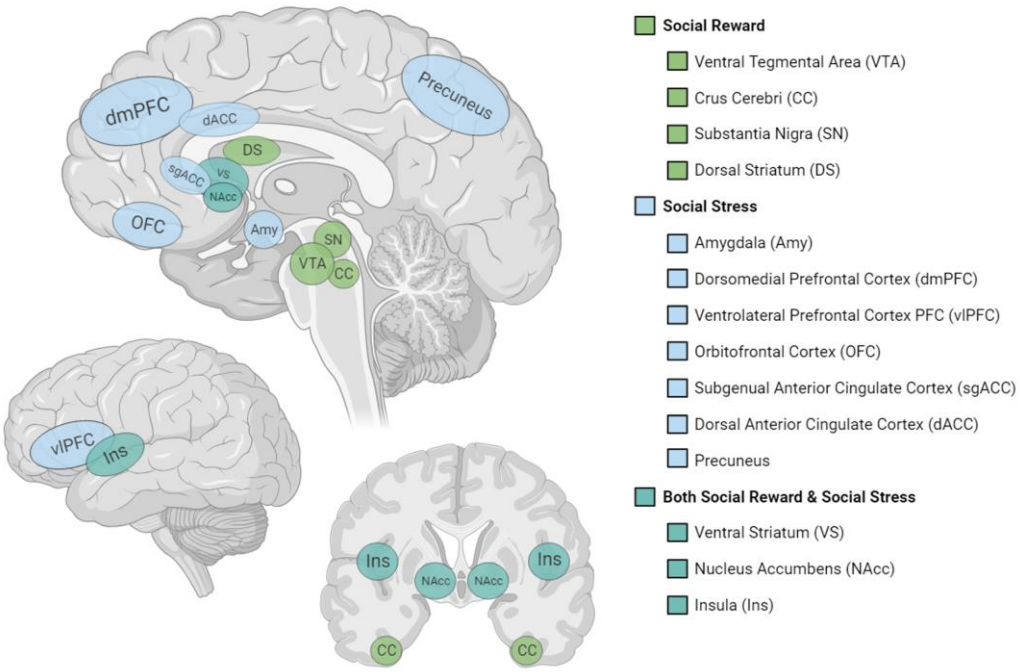
Neural Response to Rewards and Social Experiences

Given the reinforcing nature of substances, one factor key to understanding the etiology of substance use is neural reactivity to rewarding stimuli in specific regions of the brain (Squeglia & Cservenka, 2017). Problematic substance use has been associated broadly with neural response to monetary reward in the dopaminoreceptive nucleus accumbens (NAcc) within the ventral striatum (VS), as well as the ventral tegmental area (VTA), orbitofrontal cortex (OFC), medial prefrontal cortex (mPFC) including the ventromedial region (vmPFC), lateral prefrontal cortex (lPFC), and to a lesser extent, regions of the anterior cingulate cortex (ACC) and the insular cortex (Bhanji & Delgado, 2014; Edalati et al., 2018; Gray & Squeglia, 2017; Hamidullah et al., 2020). Social reward in particular has been linked to activation of the VS, NAcc, VTA, crus cerebri (CC), substantia nigra (SN), and dorsal striatum (DS) (Beard et al., 2022b). Experiences of social stress have been found to elicit activity in some of the same regions including VS, NAcc, and insula. Additionally, social exclusion and other social stressors have been linked to activity in the amygdala, dmPFC, vlPFC, OFC, precuneus, and subgenual (sgACC) and dorsal (dACC) ACC. These relevant brain regions are presented in Figure 1.1, modified from Beard et al (2022b). Activity among these networks has been discussed in

theories about substance use (Blum et al., 2000; Buckholtz et al., 2010; Cousijn et al., 2017; Ernst & Fudge, 2009; Shulman et al., 2016).

Figure 1.1

Neural Regions Activated by Social Stimuli



Note: Figure adapted from Beard et al. (2022b). Social Reward (green) refers to experiencing or perceiving social stimuli that are rewarding, such as peer acceptance or social inclusion. Social Stress (blue) refers to experiencing or perceiving social stimuli that are distressing, such as peer rejection or social exclusion. The overlap of associations between these two categories are represented in teal.

Neurobiological Theories Explaining Substance Use

Previous work on reward-related neural activity has demonstrated that substance use is associated with atypical activity in reward systems, including patterns of both hypo- and hyper-activity (Blum et al., 2015; Swartz et al., 2020). This observation supports two different, though not mutually exclusive, neurobiological theories of substance use. First, the *impulsivity theory of addiction* (Buckholtz et al., 2010; Luijten et al., 2017) asserts that hyper-reactivity to non-

substance rewards (e.g., money) can predispose individuals to seek out alternative and stronger rewarding activities, such as trying cannabis. Thus, brain activity indicative of a higher VS response to reward is hypothesized to lead to problematic substance use through greater impulsivity and sensation seeking. Second, the *reward deficiency syndrome theory* proposes that individuals with brain activity indicative of a blunted response in reward-processing regions may use substances as a means of compensating for this hypoactivation, to increase arousal to a typical level (Blum et al., 2000; Cloninger, 1987). Thus, lower VS response to reward cues is hypothesized to lead to problematic substance use through stress reactivity and internalizing symptoms. In addition, research that has linked higher alcohol and cannabis use to blunted VS response to reward (Hanson et al., 2015) suggests that motivations to use these substances could include coping with internalizing symptoms (i.e., depression and anxiety) (Conway et al., 2016; Felton et al., 2019; Hussong et al., 2011; Rappeneau & Berod, 2017). Taken together, substance use is associated with domain-general dysfunction in reward processing networks of the brain.

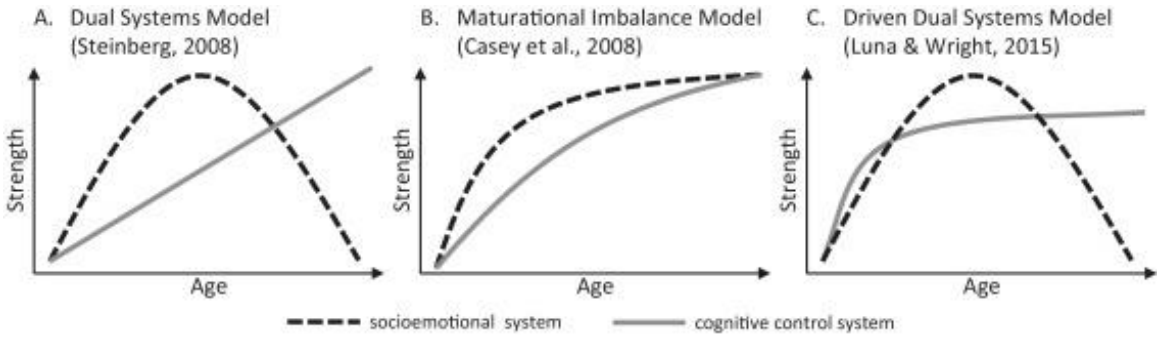
Theories Explaining Risk-Taking in Adolescents

In developmental neuroscience, "imbalance" models suggest that reward- and control-related systems of the brain mature at different rates, which creates an imbalance in the communication between them during adolescence (Shulman et al., 2016). First, the Dual-Systems Model (Casey et al., 2008; Steinberg, 2008) proposed that a "socioemotional reward system" modulating reward sensitivity and social salience fully develops by early adolescence, whereas a "cognitive control system" modulating regulation of behavior continues to develop through the mid- to late 20s. The socioemotional reward system contains dopamine-rich regions of the brain localized in the limbic and paralimbic areas, such as the VS, DS, OFC, and mPFC. The cognitive control system involves the lPFC, ACC, anterior insula, inferior frontal junction

(IFJ), and posterior parietal cortex (PPC). This pattern of neurodevelopment can be applied to adolescent substance use, as youth may seek out drugs due to their rewarding or reinforcing properties (e.g., social approval), and be less able to control impulses (e.g., binge drinking at a party), creating a "perfect storm" for substance use (Casey & Jones, 2010). Second, the Driven Dual-Systems model suggests that the neurodevelopment of socioemotional arousal follows an inverted-U shaped trajectory, whereas the neurodevelopment of cognitive control begins linearly but plateaus in mid-adolescence, rather than continuing to increase into the 20s (Luna & Wright, 2016). In this view, adolescents are able to plan and regulate behavior at the same level as adults, but they cannot yet apply these capabilities consistently, especially in emotionally charged situations. Adolescents have newfound adult-level cognition, which provides insight into their own risky decisions; but their decisions are biased in rewarding contexts, and especially in social situations. Figure 1.2 displays a comparison of different imbalance models of neurodevelopment from a review by Shulman and colleagues (2016).

Figure 1.2

Neurodevelopmental Imbalance Models of Adolescent Risk-Taking



Note: Figure from Shulman et al. (2016). Strength refers to the role that different neural systems play in adolescent risk behavior. The dashed line represents the "socioemotional" system, whereas the solid line represents the "cognitive control" system.

Third, the Triadic Model (Ernst & Fudge, 2009) expands on the dual systems concept by hypothesizing that a third brain system is important for understanding developmental differences in motivated behavior. In this model, motivated behavior originates from the interplay of two opposing social-affective neural circuits: avoidance and approach. Approach responses (e.g., moving toward happy faces) are mediated by the VS, whereas avoidance responses (e.g., turning away from angry faces) are mediated by the amygdala. Input from these two circuits is managed by cognitive regulatory circuitry in the PFC. In adulthood, the regulatory circuitry can control the other circuits, thus balancing the system. In adolescence, however, the regulatory circuitry has not matured enough to regulate the heightened motivation to approach appetitive cues, thus making the system out of balance. Substance use emerges from input "tipping" toward approach motivation circuity – and dampening of avoidance motivation circuitry – without sufficient prefrontal regulation circuitry input to control impulses.

Social Plasticity Hypothesis of Substance Use Desistance in Adulthood

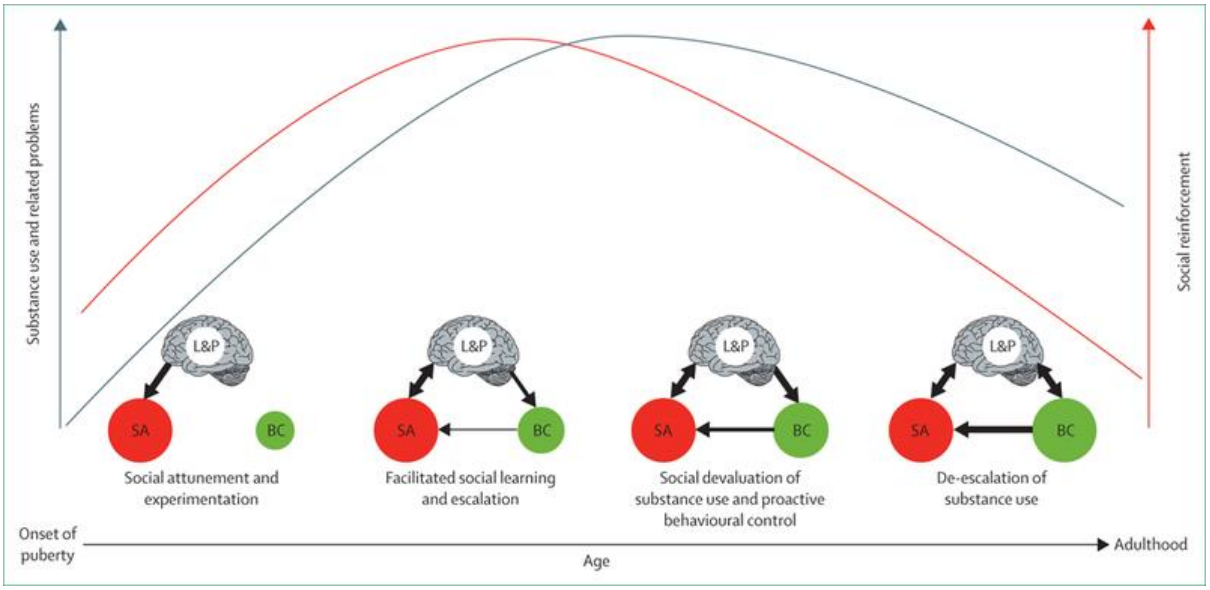
The transition from adolescence to young adulthood involves an increase in substance use as individuals reach the legal age for drinking alcohol and, in some U.S. states, purchasing cannabis; but this pattern is followed by a decrease after the age of 25 (Miech et al., 2024). Young adults take on newfound responsibilities, such as career performance and family caretaking; however, neural changes are also key, as argued in the Social Plasticity Hypothesis. Cousijn et al. (2017) proposed that there are adaptive aspects of brain development specifically during adolescence that may confer resilience against SUDs, as the same neuro-social mechanisms that place adolescents at initial risk of substance use can also lend protection. These neuro-social mechanisms include social attunement (i.e., need to harmonize with the social environment) and neural plasticity (i.e., capacity for synaptic changes from on environmental

inputs) in networks for executive control (dlPFC, PPC, dACC, inferior frontal gyrus [IFG]), salience and attention (insula, ventral ACC, OFC, VS, DS), reinforcement learning (mPFC, hippocampus, parahippocampal gyrus [PHG], VS, insula), and social cognition (temporoparietal junction [TPJ], superior temporal sulcus [STS], temporal pole, pACC, mPFC).

During young adulthood, high attunement to peers leads to the social devaluation of substance use. For example, a young adult may recognize that binge drinking is no longer as "cool" as it was previously during adolescence, and thus be less likely to engage in this behavior. This devaluation of substance use occurs alongside the optimization of behavioral control, throughout a time when brain plasticity is high. More mature functioning of associative learning mechanisms – mediated by the hippocampus and striatum – drives adaptive behavioral changes and decreases the reinforcing value of substances in young adulthood. Cousijn et al. (2017) note that individuals are more likely to decrease in substance use if their earlier use resulted from social reinforcement, such as positive peer feedback; and not from physical reinforcement, such as intoxication effects. Additionally, individuals might deviate from this normative trajectory, and timing might vary due to individual differences in social attunement, behavioral control, neuroplasticity, neural function, family history, and personality-related risk factors such as high sensation seeking. Figure 1.3 presents one aspect of this model from Cousijn et al. (2017).

Figure 1.3

Social Plasticity Hypothesis of Adolescent and Young Adult Resilience to Substance Use



Note: Figure from Cousijn et al. (2017). SA = Social Attunement, BC = Behavioral Control, L&P = Learning and Plasticity.

Across each of these theoretical models, typically-expected brain development predisposes adolescents toward risky behaviors such as substance use, but their social environments are also formative. Adolescents and young adults vary in their neural sensitivity to rewarding and social situations, as well as their experiences in peer groups and expectations of their family. Considering that adolescents spend more time with peers, social rewards and social stressors are particularly influential during adolescence and young adulthood, while the developing brain is highly sensitive to social information. Still, past research on adolescent substance use has focused heavily on non-social, such as receiving money, rather than social situations (Beard et al., 2022b). Furthermore, because past studies have relied heavily on WEIRD samples, knowledge about social environments is limited such as how aspects of familial and cultural factors contribute to substance use within other racial/ethnic groups.

The Current Studies

Guided by theories of reward and substance use neurobiology (Buckholtz et al., 2010; Blum et al., 2000), risk taking and imbalances in brain development (e.g., Shulman et al., 2016), and brain plasticity within social contexts (Cousijn et al., 2017), this dissertation investigates how substance use is associated with neural activity elicited by social and non-social reward experiences in the context of neuroimaging tasks as well as with self-reported social experiences. Study 1 investigated how neural activity to social reward and monetary reward is associated with change in substance use from mid-adolescence to young adulthood, and how change in neural activity from mid- to late adolescence is related to change in use. Study 2 examined associations among social support, social stress, and substance use, and whether those associations are explained by neural activity and peer influence. Specifically, this included testing whether (a) early experiences of social support and social stress influence later substance use, (b) early substance use influences later social functioning, (c) a bidirectional link exists between social functioning and substance use; and (d) these pathways are mediated by neural activity during social exclusion and self-reported resistance to peer influence (i.e., social susceptibility).

These two studies longitudinally examine brain-behavior relations, from mid-adolescence to young adulthood (Study 1) and from late childhood to young adulthood (Study 2). Participants in these studies were socioeconomically-diverse Mexican-origin individuals, a population under-studied in developmental neuroscience research and at higher risk of earlier and heavier substance use than other cultural or ethnic groups. Each study builds upon theoretical foundations and previous patterns of findings in the literature, while also providing new perspectives in under-researched areas, overall advancing the literature about the complexities of substance use and brain development in social contexts.

CHAPTER TWO

STUDY 1: ASSOCIATIONS AMONG SUBSTANCE USE AND NEURAL RESPONSE TO SOCIAL AND MONETARY REWARDS FROM ADOLESCENCE TO YOUNG ADULTHOOD

Adolescence has been characterized as a time of risk-taking, relative to childhood and adulthood, as evidenced by peaks in sensation seeking and risky behaviors (Shulman et al., 2016; Spear, 2011; Steinberg et al., 2018), such as substance use (Casey & Jones, 2010; Holmes et al., 2016; Tervo-Clemmens et al., 2020). Substance use has been associated with individual differences in self-reported reward sensitivity and impulsivity (Beard & Wolff, 2020; Kong et al., 2013; Poulton & Hester, 2019), as well as social factors such as resistance to peer influence (Monahan et al., 2009; Sumter et al., 2009). Functional magnetic resonance imaging (fMRI) research has provided a wealth of information about how monetary (i.e., non-social) reward-related brain function relates to substance use (Forster et al., 2018; Garrison & Potenza, 2014; Moeller & Paulus, 2017; Squeglia & Cservenka, 2017). Neural response to social reward and substance use, however, has received less attention despite the outsized influence of social context on substance use (Beard et al. 2022b). The current study was designed to test neural response to monetary reward (i.e., a non-social reward) and experiences of social acceptance (i.e., a social reward) in relation to substance use from mid-adolescence to young adulthood.

Social Influences on Substance Use

The adolescent brain does not develop in isolation, but rather in a social context that increasingly includes a peer environment of greater complexity and diversity (Blakemore & Mills, 2014; Nelson et al., 2016; Schriber & Guyer, 2016; Tousignant et al., 2017). Substance use overwhelmingly occurs in social contexts, such as a friend offering a sip of beer at a party

(Allen et al., 2012; Dishion & Tipsord, 2011; Gallegos et al., 2021; Teunissen et al., 2012). Despite a wealth of behavioral evidence that peers constitute the primary contextual risk factors for adolescent substance use (but positive peers are protective; Beard & Wolff, 2020; Coyle et al., 2016; Duell & Steinberg, 2021), few studies have directly examined how neural processing of social events predicts substance use in adolescents and young adults. Most studies involving adolescents have assessed domain-general risk-taking and different forms of social influence (e.g., having a peer observe decisions), whereas studies testing substance use have involved adults and typically compared activity between those who use substance and those who do not. Social stimuli and experiences in the context of substance use among adolescents and young adults remain an understudied and important area for future work.

The adolescent risk-taking literature has been influential in our understanding of social influences on the developing brain. In adolescents, relative to adults over the age of 25, the mere presence of a same-aged peer (i.e., implicit peer influence) has been found to increase risk-taking behaviors (Breiner et al., 2018; Gardner & Steinberg, 2005) and heighten activity in the ventral striatum (VS; a striatal region important for reward processing) and the orbitofrontal cortex (OFC; a frontal region important for reward processing) during risky decision-making (Albert et al., 2013; Chein et al., 2011; Sherman et al., 2018b). Young adults demonstrate less neural activity to reward in the VS and OFC than do adolescents while being observed by a peer, but more activity than adults over the age of 25, suggesting that the presence of a peer is still highly salient during this period of development (Albert et al., 2013). Additionally, Pei et al. (2020) revealed that more functional connectivity between the VS and salience regions (insula and anterior cingulate cortex/ACC) during risk-taking predicted safer driving in a driving simulator one week later. Further, adolescents with greater co-activation of reward and salience regions

conformed more to a peer who encouraged safe driving (e.g., driving under the speed limit), whereas adolescents with less co-activation (and higher ACC activity) conformed more to a peer who encouraged risky driving (e.g., speeding). These findings suggest that regulation of the VS by other brain regions may protect against risky peer influence. Taken together, engaging in risky behaviors in general may be more rewarding when in the context of peers, as suggested by these neural activation patterns (Braams et al., 2015). Considering the tendency for substance use to occur in peer contexts, neural response during social influence likely also predicts use.

Social processes relevant for substance use might also differ across sociodemographic groups, and involve values specific to certain cultures. Additionally, samples studied in developmental neuroimaging work have been limited in cultural, racial, and ethnic diversity. Identifying risk and protective factors important for specific sociodemographic groups is needed to design more targeted and culturally-relevant interventions for adolescent substance use. For example, familism, a Latinx cultural value centered on family closeness, can buffer against substance use. Previous behavioral work has established that high endorsement of familism is linked to less substance use among adolescents (Lardier et al., 2018). In neuroscience research, greater endorsement of familism has also been associated with lower VS response to monetary reward during risk-taking, indicating diminished reward sensitivity; and with higher dlPFC response, indicating greater cognitive control (Telzer et al., 2013). Despite vulnerability to high levels of substance use compared to other racial and ethnic groups (Atherton et al., 2016; Miech et al., 2024; Trent et al., 2023), coupled with the relevance of protective cultural factors (Lardier et al., 2018), Latinx individuals remain underrepresented in developmental social neuroscience research on risk and protective factors for substance use.

Neural response to monetary rewards has been measured most commonly with the Monetary Incentive Delay (MID) fMRI task (Knutson et al., 2000). In the MID task, participants see cues indicating potential gain or loss of one of three magnitudes of money (as well as a neutral condition, with no change in outcome) and press a button in response to a target as quickly as possible to gain money on gain trials, or to avoid losing money on loss trials. Studies that have used the MID task have identified specific brain regions recruited during anticipation of reward and punishment in adolescents, which has been linked to substance use (Bjork et al., 2004; Bjork & Pardini, 2015; Coronado et al., 2020). Both hypo- and hyper-activation of reward circuitry (including the VS and medial prefrontal cortex/mPFC) has been associated with adolescent substance use, following different pathways. For example, blunted VS response (i.e., hypo-activation) to anticipated monetary rewards has been found to predict substance use in adolescents with high novelty-seeking tendencies (Büchel et al., 2017). In contrast, heightened VS response to anticipated monetary rewards has also been identified as a correlate of substance use among young adults (Garrison et al., 2017; Morales et al., 2018; Nestor et al., 2010).

Longitudinally, Lamm et al., (2014) found that activation of the striatum – including the nucleus accumbens (NAcc), caudate, putamen, and globus pallidus – while anticipating high compared to low gain increased between the ages of 16 and 20; but other studies using different reward tasks have found no significant age-related changes between adolescence and young adulthood (Baranger et al., 2021; van Duijvenvoorde et al., 2014). Substance use has not been evaluated in this past work, but gender differences might be crucial to consider. Swartz et al. (2020) found two different pathways between boys and girls from reward response to increases in alcohol use over two years, in a sample of Mexican-origin adolescents. Greater VS and average vmPFC responses to potential monetary reward (using the MID task) were associated

with increases in alcohol use among boys, whereas blunted VS and higher dmPFC responses predicted increases in alcohol use among girls. These findings suggest that profiles involving hypo- and hyper-activation of reward regions might vary due to gender differences in neural development. It remains unknown, however, if similar patterns of neural activity would be seen in response to social rewards as are found to monetary rewards, thus revealing if both types of reward engage the same brain regions and similarly relate to substance use, or if social reward has unique properties in its engagement of brain activity and association with substance use.

Neural Response to Social Rewards

As an approach to probe neural response to social reward, the MID task was adapted into a social version. In what has been called the Social Incentive Delay (SID) task, adolescents receive social rewards (smiling faces) and punishments (scowling faces) instead of monetary gains or losses, respectively (Martins et al., 2021; Telzer et al., 2021). Using this paradigm paired with fMRI, findings indicate that seeing smiling faces relative to scowling faces elicits VS activity in adolescents. The SID has also been extended to research on substance use. Flannery et al. (2023) reported that adolescents who used substances at least once a month over one year (considered "regularly using" participants) demonstrated increases in VS response to social reward linearly over three years of annual assessments. Adolescents who engaged in substance use showed reduced VS activity to social reward during the first scan (i.e., blunted response), but their VS activity to social reward increased over time. This pattern suggests that the initiation of substance use might sensitize the brain to social rewards, which often involve the potential for positive outcomes as well as risk for negative ones.

Another proxy for social reward has been to show "likes" on photos in a task resembling the social media platform Instagram (Sherman et al., 2016; Sherman, et al., 2018a). Studies have

demonstrated significant NAcc activity in response to many likes (versus few), a putative socially rewarding cue, consistent with reported patterns of neural response to monetary rewards. Further, VS response to likes was positively correlated with age among high school students, but not among college students, reflecting an age-related pattern of reduced sensitivity to this type of social reward in young adulthood. Such findings are relevant in the context of results from other studies that have shown attenuated neural response to reward when being observed by peers among adolescents, as compared to young adults and adults over the age of 25 (Albert et al., 2013). Findings of decreased social influence on risky behaviors and associated neural correlates across this period also aligns with predictions from the social plasticity hypothesis (Cousijn et al., 2017), although research involving likes has not assessed substance use directly.

Being accepted and included by one's peers is an inherently rewarding experience for adolescents, given that humans have a core need to belong and that adolescents' peers play a vital role in forming one's identity and ability to establish healthy romantic relationships (Guassi Moreira et al., 2018; Lee et al., 2017; Silva et al., 2015; Smith et al., 2015). In addition to neuroimaging studies that used the SID and Instagram tasks, there is evidence that social acceptance activates similar neural circuitry and in the same magnitude as monetary reward (Jarcho et al., 2022; Jarcho & Nelson, 2019; Sazhin et al., 2020). Adolescents show strong striatal response to acceptance (Guyer et al., 2012; Weinberg et al., 2021), suggesting that it is a potent social reward. Another method of measuring social reward and punishment is with the Cyberball fMRI task (Eisenberger & Lieberman, 2003; Williams & Jarvis, 2006), a ball-tossing game in which the participant is included and then excluded from the game after a predetermined number of ball tosses. Cyberball has frequently been used to examine neural activation during social exclusion, as it robustly activates neural regions that support social salience and distress

related to social exclusion (Mwilambwe-Tshilobo & Spreng, 2021; Rotge et al., 2015; Vijayakumar et al., 2017). In work on substance use, Gilman et al. (2016a) found that college students who regularly used cannabis (2-4 times per week but not daily) had less neural response to social exclusion in the insula than non-using control participants. This pattern suggests that cannabis use may lead to reduced sensitivity to negative social information. Neural response to inclusion trials in Cyberball, however, has not yet been studied in the context of substance use. Thus far, evidence has indicated that brain regions supporting reward and salience detection code acceptance experiences as rewarding and rejection experiences as distressing, consistent with self-reported experiences; but substance use might alter these effects.

Indeed, substance use could potentially lead to a blunted response to the positive prospect of social rewards. In one investigation, Jarcho et al. (2022) examined neural response to receiving both monetary reward and social reward in 33 college students. The social reward task involved viewing photographs of two peers' faces and guessing which peer liked them, before receiving feedback of either a green arrow pointing upward as reward (meaning the participant chose the peer who liked them) or a white horizontal dash as non-reward (meaning the participant chose the peer who never rated them). Reduced activity in the right VS in response to experiencing a socially rewarding outcome (learning the peer liked them) was associated with greater substance use behaviors, opposite to what was found when receiving a monetary reward, in which heightened VS activity was linked to more use. Greater VS response to positive social feedback is normative during adolescence and young adulthood (Dalgleish et al., 2017; Rudolph et al., 2021); thus, it is plausible that individuals who do not recruit these neural systems during positive social encounters seek appetitive experiences through other avenues, such as substances

(Jarcho et al., 2022). This interpretation is in alignment with the reward deficiency syndrome view of substance use and addiction (Blum et al., 2015).

Lastly, two other approaches to assessing response to social reward involve physical touch and observing social interactions. Zimmermann et al. (2019) adapted an interpersonal touch task to assess how heterosexual men (aged 18–35) with cannabis dependency ($n = 23$) compared to non-dependent men ($n = 24$) responded to physical touch from an attractive female experimenter. In this paradigm, the experimenter either stood far away from the participant, close to the participant, or administered repeated soft touches to the participant's shins. Cannabis users showed decreased dorsal striatal (DS) response to touch from the female experimenter, whereas non-users showed increased DS response to being touched. One interpretation is that the link between cannabis dependence and blunted striatal processing of social rewards signifies a deviation from typical striatal responding, which contributes to interpersonal deficits. Conversely, another study used non-social stimuli (i.e., abstract shapes) to study neural response to socially-imbued interactions in relation to substance use. Participants in the Human Connectome Project (HCP) completed a task involving watching shapes interact, either in a pattern representing social interaction, or a pattern of random movement (Li et al., 2021). Binge drinkers aged 22–36 demonstrated less response in the mOFC and precuneus to social interactions among shapes. Although this study involved abstract shapes (rather than human faces or other explicitly social stimuli), it is worth noting that heavy drinkers showed altered engagement when viewing social interactions in this controlled setting.

In conclusion, a robust neuroscience literature indicates that substance use is linked to atypical activation of reward regions in the brain in response to monetary, non-social rewards. A nascent literature suggests that social rewards activate similar reward circuitry as non-social

rewards. Regarding substance use, however, only two studies to my knowledge (Flannery et al., 2023; Jarcho et al., 2022) have assessed neural response to social rewards within the context of substance use. Moreover, only Jarcho et al. (2022) have directly compared neural response to both social and non-social rewards. What remains to be known is how these patterns might differ in adolescents, and how these associations change longitudinally from adolescence into young adulthood.

The Current Study

While past work has characterized associations between neural response to monetary reward and substance use, little is known about how neural response to social reward is associated with substance use, especially during adolescence and the transition into young adulthood. The current study assessed if neural response to social inclusion (a salient social reward) at ages 17 and 19 was related to substance use, both concurrently and longitudinally from ages 16 to 21. I assessed both recent use during the past three months, and longer-term use during the past two years, to comprehensively capture changes in substance use over the five-year period. Substance use was also modelled as both latent and observed. Latent modeling involves the benefits of reduced estimation bias, and reduced number of parameters in complex models; however, a series of regression analyses were also conducted with arithmetic change scores, to address hypotheses involving rate of change in neural activity and substance use over time. Data resulted from two timepoints of neuroimaging collected at ages 17 and 19, and three timepoints of substance use data collected at ages 16, 18, and 21. Neural response was examined specifically in the NAcc and the mPFC, given their consistent implication in the processing of monetary reward (e.g., Bjork et al., 2004). The VS, which contains the NAcc, also processes social reward (e.g., Flannery et al., 2023).

Hypotheses centered on longitudinal changes in neural activity, and associations with substance use. Regarding neural activity, hypotheses were as follows: (1) social inclusion will elicit activity in the NAcc and mPFC at both ages (17 and 19), and this activity will be positively associated with that of monetary reward, (2) NAcc response to reward will be positively associated with mPFC response to reward within each task, (3) neural response to social inclusion will decrease from ages 17 to 19, reflecting a developmental pattern in which social reward is more salient during adolescence than in young adulthood, and (4) neural response to monetary reward will also decrease with age. Regarding neural activity in relation to substance use, hypotheses were as follows: (5) greater activation of the NAcc and mPFC to social inclusion and monetary reward will be associated with greater concurrent substance use, (6) greater NAcc and mPFC response to social inclusion and to monetary reward at ages 17 and 19 will predict greater substance use at ages 18 and 21, respectively, (7) greater NAcc and mPFC response to social inclusion at age 17 will predict more change in substance use by age 19, such that higher social reward response will be associated with a steeper increase in substance use, and lastly, (8) more change in neural response to social inclusion will predict more change in substance use, such that adolescents with a steeper decrease in NAcc/mPFC response to social inclusion (i.e., more change) will demonstrate a more gradual increase in substance use (i.e., less change) across two years. In other words, less social reward responsivity over time might offset the typical trend of substance use increasing between mid-adolescence and young adulthood. Finally, given the gender differences revealed by Swartz et al. (2020), an exploratory hypothesis was that (9) the associations between neural responses and substance use might differ by gender. Boys with greater NAcc response to monetary reward might show increased substance use, whereas girls

with greater mPFC response might show increased substance use; but no directional hypotheses were made about gender differences in neural response to social reward specifically.

Method

Participants

Participants included 289 Mexican-origin adolescents recruited into two neurobiology substudies of the California Families Project (CFP), an ongoing longitudinal study of children and their families. As described in previous publications (Beard et al., 2022a; Johnson et al., 2021; Schriber et al., 2018; Swartz et al., 2020; Weissman et al., 2015), participants in the original CFP main study included 674 Mexican-origin families with a child in the fifth grade (M_{Age} = 10.4 years, *SD* = 0.61, 50% girls) drawn at random from school rosters in Sacramento and Woodland, California. The depression substudy was designed to examine neurobiological mechanisms of depression risk in adolescents, and the substance use substudy was designed to examine neurobiological mechanisms of substance use risk. Both substudies included two time points of MRI data collection approximately two years apart, hereafter referred to as time 1 and time 2, respectively. Data collection for the CFP main study occurred within the same years, as well as a third time point approximately two and a half years after time 2, hereafter referred to as time 3 (see Procedures).

Depression Substudy

The depression substudy enrolled 229 adolescents (M_{Age} at scan = 17.16 years, *SD* = 0.44, range = 16.24-17.97 years, 49.3% girls) at time 1 (Beard et al., 2022a; Schriber et al., 2018). This substudy oversampled youths with elevated (but sub-clinical) levels of depressive symptoms. Depressive symptoms were self-reported by adolescents during the 9th grade (age 14-15 years) with the computerized Diagnostic Interview Schedule for Children-IV (DISC-IV) (Shaffer et al.,

2000) and the General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (MASQ) (Watson et al., 1995). The sample included adolescents whose symptom scores ranged above the median on all three measures of depression (n = 43), two measures (n = 64), or one measure (n = 68); and at or below the median on all three measures (n = 54) to achieve variability. No participants met the diagnostic criteria for Major Depressive Disorder at the time. A variable was created to dichotomize adolescents into "low risk" (n = 71) and "elevated risk" (n = 158) categories, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized DISC-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the MASQ (Watson et al., 1995). This variable is hereafter referred to as "depression recruitment status." The Cyberball (Williams & Jarvis, 2006) and Monetary Incentive Delay (MID) (Knutson et al., 2000) tasks were administered during both time points of the depression substudy.

At Time 1 of the depression substudy, 10 adolescents were ineligible for MRI scanning due to contraindications (e.g., braces), and two were excluded due to equipment malfunction (e.g., shutdown of the stimulus computer), yielding 217 adolescents who completed MRI scans. For the Cyberball task, 21 adolescents were excluded from analyses for reasons of data quality, such as excessive head motion defined as movement of more than 1 mm from previous repetition time (TR) on more than 20% of TRs, resulting in 196 adolescents with high-quality Cyberball scan data. For the MID task, 24 participants were excluded from analyses for reasons of data quality, and one was excluded for poor task performance defined as less than 10% success on gain trials, resulting in 192 participants with high-quality MID data.

Of the 229 adolescents recruited for time 1 of the depression substudy, 167 returned for the Time 2 assessment approximately two years later; and 10 new participants were added during

time 2, yielding a total of 177 participants (M_{Age} at scan = 19.82 years, *SD* = .40, range = 18.28-19.95 years, 52% girls). Ten participants were ineligible for scanning due to MRI contraindications, and five had unavailable neuroimaging data, resulting in 162 individuals who completed the Cyberball task scan and 144 who completed the MID task scan (9 participants finished Cyberball but not the MID). For the Cyberball task, 11 participants were excluded from analyses due to data quality, yielding 151 with high-quality scan data. For the MID task, 9 participants were excluded for data quality, yielding 144 with high-quality scan data. Lastly, the 10 participants who completed time 2 scans but not time 1 scans were excluded from longitudinal analyses, yielding a total of 141 participants with two time points of Cyberball task scan data, and 134 with two time points of MID task scan data (see Figure 2.1).

Substance Use Substudy

The substance use substudy at time 1 initially included 90 adolescents (M_{Age} at scan = 16.26 years, *SD* = 0.50, range = 15.58-16.79 years, 55% girls) (Chahal et al., 2021; Weissman et al., 2015). The substudy recruited adolescents based on their responses to two substance use questionnaires (Elliott et al., 2006; Shaffer et al., 2000) in the 9th grade. Adolescents met criteria for the substance-using group (*n* = 47) if they reported using alcohol, cannabis, or other drugs three or more times within the three months before their annual CFP main study assessment (Chahal et al., 2021; Venticinque et al., 2021; Weissman et al., 2015). Adolescents met criteria for the abstainer group (*n* = 43) if they reported never using substances and having no intention to in the future. These criteria were used in simple random sampling without replacement to select an equal proportion of users and abstainers, ensuring variability in substance use. Time 1 rates of substance use were mostly subclinical, but four adolescents met criteria for a diagnosis of alcohol use disorder, two met that of alcohol dependence, one met that of cannabis use

disorder, and one met criteria for cannabis dependence. Overall, patterns of use were similar to distributions found among Latinx youth, including those in the CFP main study (Clark et al., 2020; Atherton et al., 2016; Cruz et al., 2019; Parrish et al., 2016).

At time 1 of the substance use substudy, 11 participants were ineligible for scanning due to MRI contraindications, and 6 did not complete the scan due to equipment malfunction, yielding 73 participants who completed the MID task scan. Two participants were excluded from analyses for reasons of data quality, and one was excluded for poor task performance, resulting in 70 participants with high-quality MID task scan data. Of the 90 participants recruited for Time 1 of the substance use substudy, 46 returned for the Time 2 assessment approximately two years later (M_{Age} at scan = 19.01 years, *SD* = .54, range = 18.28-20.11 years, 52% girls) (Venticinque et al., 2021). The sample size was limited by budget constraints. Three participants did not complete the MID task, and 8 were excluded from analyses for reasons of data quality, yielding 35 participants with high-quality MID task scan data.

Combined MID Sample from Both Substudies

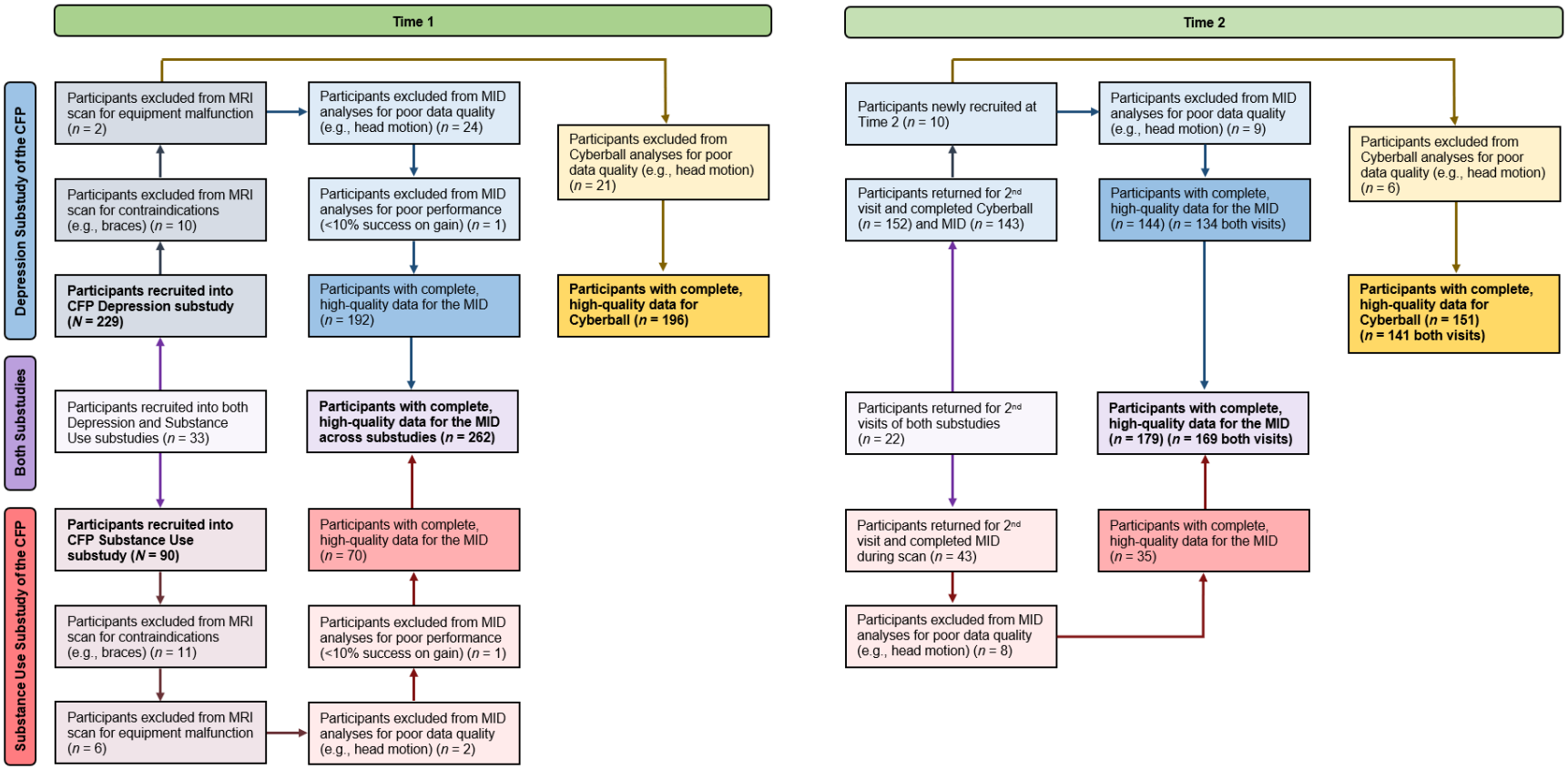
The MID was administered at both time points of both the depression and substance use substudies, allowing for a combined sample. Although the Cyberball task was also administered at both time points of the substance use substudy, the task was modified substantially in preparation for collection of data in the depression substudy; thus, participants' data could not be combined across the two substudies. Swartz et al. (2020) reported findings from the MID fMRI task collected at time 1 for the combined sample of both the depression and substance use substudies, which yielded 262 adolescents with high-quality fMRI data (192 from the depression substudy and 70 from substance use substudy).

The Current Study Sample

The present study is the first to analyze time 2 MID data from the combined sample, as well as time 2 Cyberball data from the depression substudy sample. Figure 2.1 presents the various sample sizes across substudies and time points. Of the 146 participants who completed both time points of the Cyberball task scan, 26 did not complete the MID task scan at both time points. In total, the final sample size included 120 participants who completed both time points of both the Cyberball and MID tasks. Table 2.1 displays sample demographics for these participants.

Figure 2.1

Flowchart of Sample Sizes for the Depression and Substance Use Substudies of the California Families Project



Note: CFP = California Families Project, MID = Monetary Incentive Delay. Depression refers to a substudy of the CFP examining the neurobiological mechanisms of depression, and Substance Use refers to a substudy examining the neurobiological mechanisms of substance use. Time 1 refers to the first study visit when participants were approximately 17 years old, and Time 2 refers to the second visit when participants were approximately 19 years old. Poor MRI data quality included artifacts such as ghosting, aliasing, and excessive head motion defined as movement of more than 1 mm from previous repetition time (TR) on more than 20% of TRs. Poor MID task performance was defined as less than 10% success on Gain trials.

Table 2.1

Sample Demographics

Variable	*N*	*M (SD)*
Gender	Women = 62	
	Men = 58	
Generational Status	1st Gen = 31	
	2nd Gen = 74	
	3rd Gen = 15	
Household Annual Income	< $25,000 = 36	
	$25 – 40k = 41	
	$40 – 55k = 21	
	$55 – 80k = 12	
	> $70,000 = 5	
Age at Time 1 MRI Scan		17.22 (.41)
Age at Time 2 MRI Scan		19.19 (.44)
Maternal Education in Years		9.67 (3.29)
Household Size		5.44 (1.57)

Note: $N = 120$. 1st Gen = Child born in Mexico, 2nd Gen = Child born in U.S. and at least one parent born in Mexico, and 3rd Gen = Child and both parents born in U.S. Participants were enrolled in two neurobiological substudies of the California Families Project. All variables were reported at Time 1 when participants were approximately 17 years old.

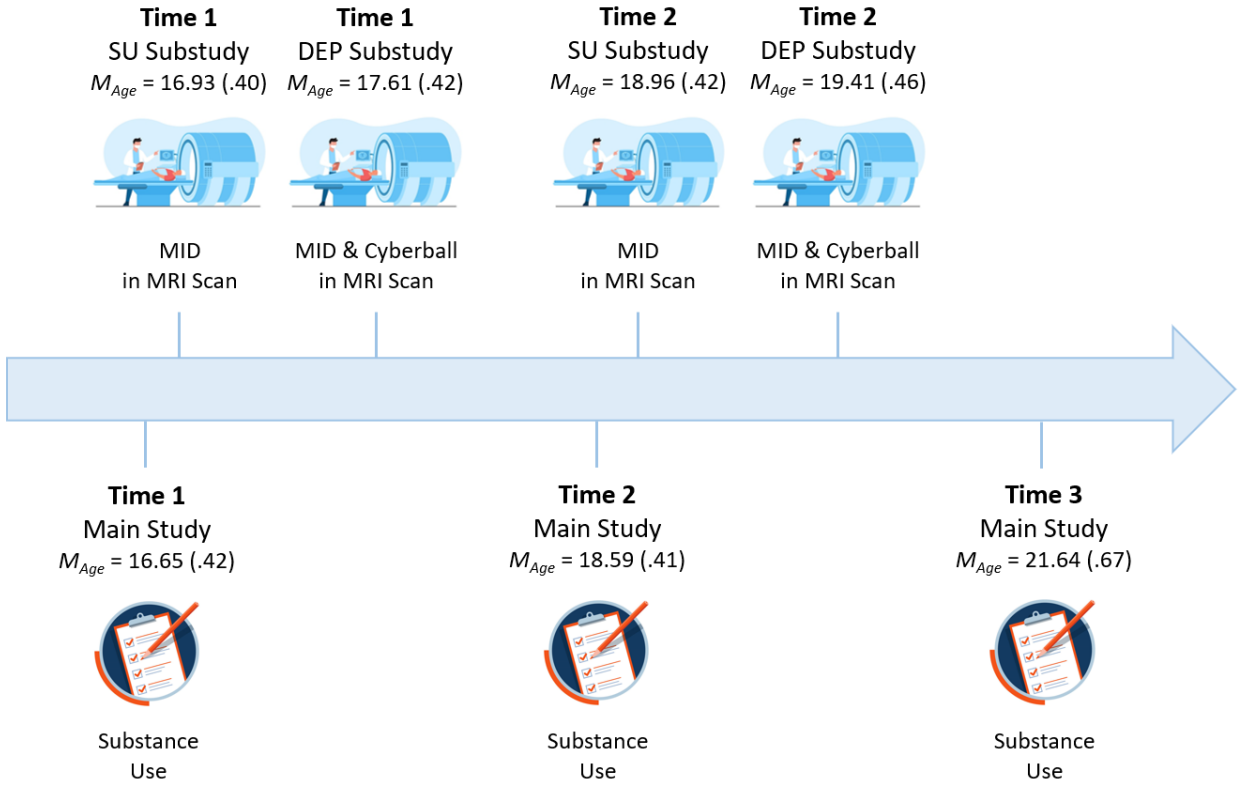
Procedure

During each MRI substudy visit, all parents gave written informed consent and youths gave assent; when youths returned for time 2 they provided written informed consent if they were 18 or older. At the time 1 assessment of the depression and substance use substudies of the CFP, adolescents and one parent visited a research facility in Sacramento, California, where the adolescent participated in an MRI scan composed of a structural scan and three tasks. At the time 2 assessment approximately two years later (see Table 2.1 for average ages in the sample of

120), participants returned for a second study visit. Substance use was assessed independently of MRI visits during the CFP main study visit. Time 1 substance use was collected an average of 5.67 months (*SD* = 2.81) before the MRI substudies, time 2 an average of 5.96 months before (*SD* = 2.92), and time 3 an average of 29.45 months after (*SD* = 2.12) the MRI study visits. All analyses in the present study controlled for age, as described in a later section. Figure 2.2 shows the timing of data collection across the CFP main study and two neurobiological substudies. At each study visit, families were compensated with $160 for their participation. All studies were approved by the institutional review board.

Figure 2.2

Timeline of Data Collection



Note: *N* = 120. DEP = Depression neurobiological substudy of the California Families Project, SU = Substance Use neurobiological substudy of the California Families Project, Main Study = California Families Project parent study from which participants were enrolled into the

neurobiological substudies, MID = Monetary Incentive Delay task assessing neural response to monetary reward, and M_{Age} = Mean age. Values in parentheses reflect standard deviation.

Measures

Substance Use

Substance use was evaluated with the Alcohol, Tobacco, and Other Drugs (ATOD) survey (Elliott et al., 2006). Participants responded to questions about their use of six different substances in the past three months: cigarettes, cannabis, beer, wine or wine coolers, hard liquor, and occasions of 5 or more drinks in a row within a few hours (binge drinking) (see Supplement A1 in Appendix A for the survey given to participants). For example, participants responded yes or no to the question, "Have you ever used or tried marijuana —also called a jay, or pot, weed, grass, hash, bud?" If the participant answered *yes*, the follow-up question was, "In the past 3 months, how many times have you used or tried marijuana?" The questions about alcohol use specified "more than just a few sips." Response options included: 1 (*Never*), 2 (*Less than Once per Week*), 3 (*About Once per Week*), 4 (*Two to Three Times per Week*), and 5 (*Almost Every Day*). Refusal to answer was coded as 8 and "Don't know" was coded as 9, both treated as missing. Valid responses were recoded to range from 0 (*Never*) to 4 (*Almost Every Day*). Answering "no" to a question about ever trying a substance resulted in a score of 0 for past 3 months' use. Higher scores represent greater use of substances. Responses to the first set of questions about ever trying a substance had rates similar to those of previous analyses of the CFP main study data at time 1 (Atherton et al., 2016; Clark et al., 2020; Cruz et al., 2019).

Analyses were separated into past-3-months substance use and past-2-years substance use, to comprehensively assess change in substance use across two different timescales from adolescence to young adulthood. Past 3 months use resulted from questions about recent use during the past 3 months. Past 2 years use resulted from questions about any occasion of

substance use at any period in one's lifetime, inherently controlling for lifetime substance use by the previous time point; for example, analyses testing change in lifetime substance use from time 2 to time 3 controlled for lifetime use by time 1. Thus, "lifetime use" captures substance use during the past 2 years, hereafter referred to as past 2 years use.

Additionally, analyses were separated into latent and composite representations of substance use. Latent substance use was composed of indicators for each substance type; for example, the latent factor for past-3-months substance use at time 1 included past-3-months occasions of cigarettes, cannabis, beer, wine, liquor, and binge drinking as observed indicators. To assess change in substance use via regression analyses, composite variables were also created by summing responses to all substance types for each time point. For example, the sum of past-3-months of substance use at time 1 included the sum of responses to all substance use items during that period of data collection. Swartz et al. (2020) created similar composite scores for the past-3-months of alcohol use. In the current study, the maximum score possible for past 3 months use was 72 (6 substances X 4 response for daily/almost daily use X 3 time points). For past 2 years use, the maximum score possible was 36 (6 substances X 2 response options for yes/no X 3 time points). Both time ranges of substance use were included to comprehensively assess both recent substance use, and more occasional use since the previous time point. To control for previous history of use, a dichotomous variable was also calculated for lifetime use by age 14 for all participants and entered as a covariate into analyses. This covariate was included to prevent a potential confound of early substance use; for instance, adolescents who reported higher use at age 16 could have either recently started using, or continued their previous use before age 16.

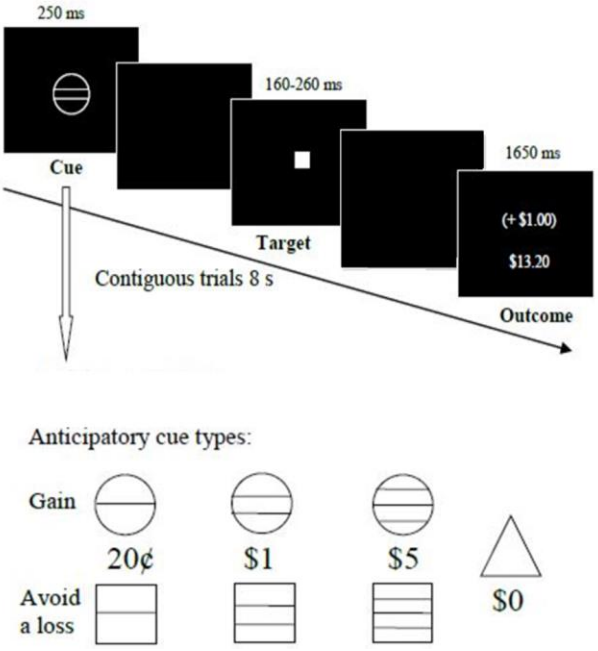
Monetary Incentive Delay Task Design

The MID task (Knutson, et al., 2001) was completed during an MRI scan to assess neural response to monetary rewards, and was programmed and presented with E-Prime computer software version 2.0 (Psychology Software Tools, Pittsburgh, PA). Figure 2.3 presents the MID task design used in the current study, adapted from Bjork et al. (2008). The MID task included two runs that each were 10.44 minutes, yielding a total of 140 contiguous trials. On a given task trial (8 sec each), participants first saw an incentive cue indicating potential gain (circle; $n = 60$) or loss (square; $n = 60$) of one of three magnitudes of money, or a neutral cue (triangle; $n = 20$) signaling no money at stake. A single line, two lines, or three lines within the cue represented the varying incentive magnitudes. This cue was followed by a jittered screen showing a cross-hair fixation point, and then a response target.

Participants were asked to press a button in response to the target as quickly as possible to gain money on gain trials, or to avoid losing money on loss trials. Participants then received feedback (1650 ms) about the amount of gain or loss, or that no change occurred. A cumulative dollar amount was also displayed on each feedback presentation. Trial type order was completely random within each run. Task difficulty was tailored to each participant's ability by adjusting target duration on the task such that participants succeed on approximately 66% of their responses using mean reaction time (RT) and accuracy rate from an earlier practice task in a mock scanner. The current study analyzed data from the contrast of Gain Anticipation > Neutral Anticipation, with gain resulting from an average across the three magnitudes of possible reward. Although the feedback/receipt phase of monetary reward might be more comparable to receipt of ball tosses in Cyberball, the anticipation phase better captures motivation to seek out rewards, which is highly relevant for motivational processes involved in substance use.

Figure 2.3

Monetary Incentive Delay Task Design



Note: ms = milliseconds, s = seconds. In the MID task, participants first see a cue indicating the amount of money to be gained or lost, then see a target to which they respond with a button press, and then see the outcome of that trial along with a cumulative running total of their winnings thus far. Cues indicated both valence (Gain, Loss, Neutral) and Magnitude (Small, Medium, Large) of the potential reward or loss.

Cyberball Task Design

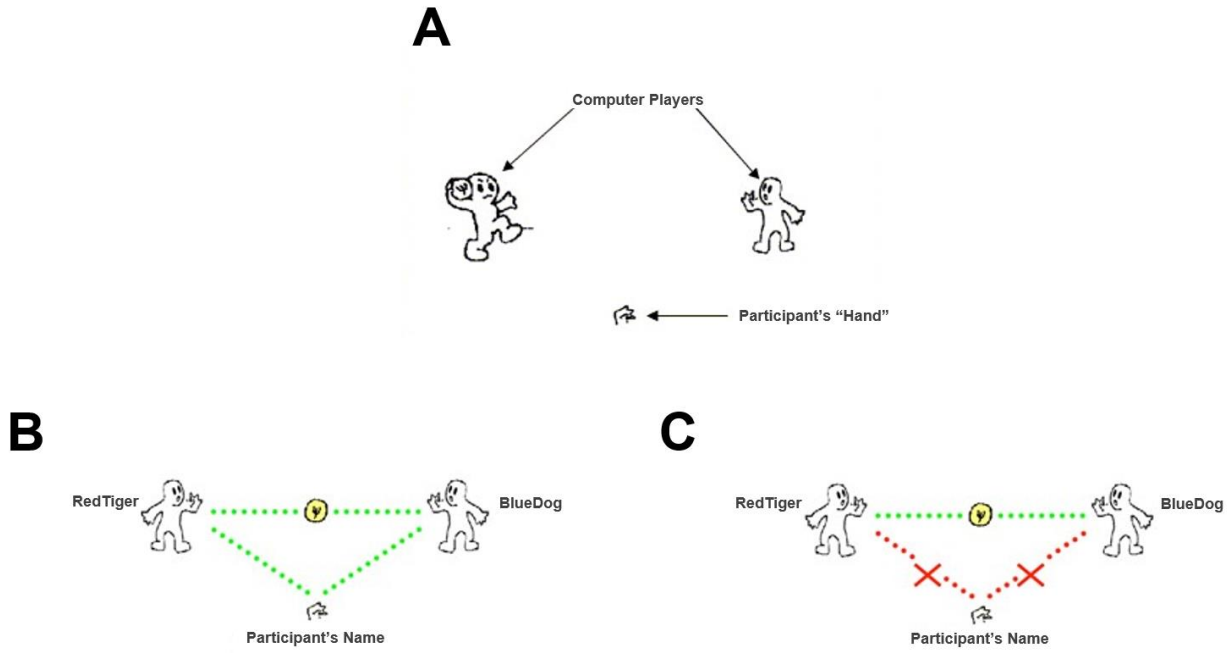
A variation of the Cyberball task (Eisenberger & Lieberman, 2003) was completed during an MRI scan to measure neural response to social inclusion, as a form of social reward. Figure 2.4 shows the adapted Cyberball task design used in the current study, as described in past work reporting on neural response to social exclusion at time 1 (Beard et al., 2022a; Johnson et al., 2021; Schriber et al., 2018). Participants were told they would play a virtual ball-tossing game with two computerized players, and were asked to imagine, as vividly as possible, that they were playing with other individuals of the same age. On the screen, participants saw cartoon figures and usernames representing two other players (of no apparent gender or race/ethnicity),

their own cartoon “hand” controlled via a button box, and a username chosen during this session. During the game, the ball was thrown back and forth among all three players. Participants chose the recipient of their throws using the button box, whereas throws of the two other players were selected by the computer program.

Participants played 12 rounds of Cyberball, with six rounds of Inclusion and six rounds of Exclusion, always presented in the same pseudorandom order: Inclusion, Exclusion, Inclusion, Inclusion, Exclusion, Inclusion, Exclusion, Inclusion, Exclusion, Exclusion, Exclusion, and Inclusion. Throughout Inclusion rounds, the other players were equally likely to throw the ball to the participant or each other. However, during Exclusion rounds, near the beginning of the round, the other players stopped throwing the ball to the participant and continued throwing it only to each other. Each round lasted 36 sec, being comprised of a fixation point (4 sec), “Begin Match!” notification (2 sec), and 10–11 ball tosses of game play (22–23 sec) that included all relevant players’ ball tosses, followed by a short reloading screen (7–8 sec). There were also Instructions (8 sec) at the start and a “Thank you!” (3 sec) at the end signifying completion of the task. The functional scan lasted 7 min 23 sec implemented in one run.

Figure 2.4

Cyberball Task Design



Note: The Cyberball task presents the participant with two computer players and a representation of their own cartoon hand (A). Inclusion trials (B) involve the participant receiving ball tosses from the other two players, whereas Exclusion trials (C) involve the two other players passing the ball to each other and leaving out the participant. Avatar names were randomly generated and included no information about gender, race, ethnicity, or other identifying features.

MRI Scan Procedures, Structural Acquisition, & Analysis for Both Tasks in Both Substudies

Participants were asked to abstain from using any substances 48 hours prior to their MRI scan visits. To check for scanning contraindications, participants completed a metal screening form, and those who indicated that they might be pregnant took a pregnancy test. To screen for current presence of substances (for the substance use substudy), participants reported on their substance use in the three days prior to the scan before being administered an oral fluid drug screen test and breathalyzer to detect drug and alcohol use in the past 24 hours. Participants were then instructed about and trained on both of the tasks, and completed a practice session in a mock MRI scanner to acclimate to the scanning environment. Once inside the scanner, adolescents

were given extensive instructions to remain still to decrease head motion, which was also limited with foam padding around the head and surgical tape markers on the face.

Participants underwent scanning on a research-dedicated 3T Siemens Tim Trio whole-body MRI system (Siemens Medical Solutions, Erlangen, Germany) with a 32-channel head coil. Following sagittal localization and a manual shim procedure, a high-resolution structural scan was acquired using a T1-weighted standardized magnetization-prepared spoiled gradient recalled echo pulse sequence, with 208.95-mm slices, a repetition time (TR) of 2500 ms, a time-to-echo (TE) of 4.33 ms, a field-of-view (FOV) of 243 mm with a 7-degree flip angle, an inversion time of 800 ms, and a 256 x 256 mm matrix. Whole-brain BOLD functional T2*-weighted echo-planar images (EPI) were acquired for each brain volume for each task (see task specific details below).

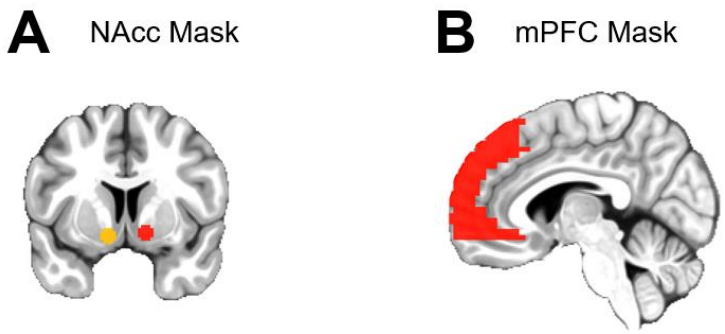
All preprocessing and data analyses were conducted using Analysis of Functional NeuroImages (AFNI: www.afni.nimh.nih.gov/afni, version 16.2.09; Cox, 1996), and with consistent analysis steps applied to both time 1 and time 2 data. Preprocessing of EPI data for both tasks included slice time correction, motion correction, re-slicing to a 1-mm isotropic voxel (1x1x1), spatial smoothing using a 6-mm full-width half-maximum Gaussian kernel, and normalization of BOLD signal intensity to percentage signal change. Functional data for each participant was then co-registered with their structural images and normalized to Montreal Neurological Institute (MNI) stereotaxic space. Volumes with head motion >1 mm from the previous volume were censored during further processing. Participants with head motion >1 mm from the previous TR on more than 20% of TRs were excluded from second-level analyses.

Second-level analyses were structural region-of-interest (ROI) analyses with the same regions for both tasks. ROIs included four striatal regions: left and right NAcc, and left and right

mPFC (Figure 2.5 shows masks created for use in both MID and Cyberball analyses). ROIs for the NAcc were based on bilateral spheres with a radius of 3.5 mm created at the locations of the left and right NAcc (MNI coordinates: x = ± 12, y = 8, z = -10). Mean contrast values of percent signal change in activation to anticipated rewards were generated for all voxels within each of the four ROIs. Left and right values were averaged together within each ROI, resulting in two values: NAcc response and mPFC response. Outliers for NAcc and mPFC activity were winsorized to within 3 *SD* of the mean.

Figure 2.5

Masks Created for Region-of-Interest Analyses of Monetary and Social Rewards



Note: NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, and ROI = Region of interest. Time 1 refers to the first study visit when participants were approximately 17 years old, and Time 2 refers to the second visit when participants were approximately 19 years old.

MID fMRI Acquisition & Analysis

For the MID task, the functional scans consisted of 320 contiguous T2*- weighted echo planar imaging whole-brain volumes including 35 interleaved 3.5 mm thick slices per brain volume, oriented to the anterior commissure and posterior commissure line and encompassing the entire cerebrum and the majority of the cerebellum. Scan parameters were as follows: 64 x 64 matrix; TR = 2000 ms; TE = 27 ms; flip angle = 80º; FOV = 224 mm; and voxel size 3.5 x 3.5 x 3.5 mm. Four acquisitions were obtained before each task onset, to allow for signal stabilization.

First-level analyses involved multiple regression models, with regressors for each event type (incentive cues, target cue, feedback), six motion parameters as regressors modeling effects of residual motion (translational displacements along the X- Y- and Z- axes, and rotational displacements of pitch, yaw and roll), and two regressors modeling baseline and linear trends per run. Regressors of interest were statistically modeled using a gamma-variate basis function convolved with a prototypical hemodynamic response function. Idealized signal time courses were estimated from the onset time of each event type. A general linear model was then used to determine the beta value and *t*-statistic for each event at each voxel. For second-level ROI analyses, four contrasts of interest were created for anticipation of monetary gains in the ROIs: combined gain (collapsed across magnitudes), small gain, medium gain, and large gain, each compared with no change (neutral condition). The contrast of interest for the current study was combined Gain Anticipation > Neutral Anticipation.

Cyberball fMRI Acquisition & Analysis

For the Cyberball task, the functional scans consisted of 126 contiguous T2*- weighted echo planar imaging whole-brain volumes including 35 interleaved 3.5 mm thick slices per brain volume, oriented to the anterior commissure and posterior commissure line and encompassing the entire cerebrum and the majority of the cerebellum. Scan parameters were as follows: 64 x 64 matrix; TR = 2000 ms; TE = 27 ms; flip angle = 80°; FOV = 224 mm; and voxel size = 3.5 x 3.5 x 3.5 mm. The first two volumes were discarded to allow for equilibration of saturation effects.

For first-level analyses, Cyberball was modeled as a block design consisting of Inclusion or Exclusion conditions. The time series of 126 image volumes was deconstructed into five regressors, each included in the design matrix. These consisted of Inclusion, Exclusion, instruction screen, “Begin match!” screen, and button presses (mostly during Inclusion) to

control for motor activity. The last three were regressors of no interest. Exclusion and Inclusion were modeled as boxcar functions with an amplitude of 1 using AFNI's duration modulation (dmBLOCK) to account for duration variability due to reaction time differences. Other regressors of interest were modeled using gamma functions. All were convolved with a canonical hemodynamic response function. The six motion parameters were modeled as effects of no interest to account for variance due to head movement. Finally, time periods showing the beginning fixation point, end reloading, and final "Thank you!" screens were not modeled to maintain an implicit baseline. Linear contrasts were calculated that compared blood-oxygen level–dependent (BOLD) responses in the Inclusion > Baseline conditions for each participant. For second-level ROI analyses, mean values of beta coefficients were extracted for Inclusion > Baseline for each ROI.

Data Analysis

Statistical analyses were conducted in RStudio version 2023.6.0.421 (Posit Team, 2023) and SPSS Statistics version 28.0 (IBM Corp, 2021). All study variables were checked for outliers and non-normality, and outliers were winsorized to within 3 *SD* of the mean before being entered into further models. Covariates included gender, age, previous substance use before age 14 (to control for effects of early substance use), and depression recruitment status (to control for effects of depressive symptoms). Previous substance use before age 14 was calculated for all participants across both substudies, along with depression recruitment status which was calculated for substance use substudy participants using the same criteria as was used for the depression substudy. Preliminary analyses included zero-order correlations and simple regressions. Main analyses included cross-lagged panel models (CLPMs) using latent substance use, and bilateral NAcc and mPFC response to social reward and to monetary reward collected

using the Cyberball and MID tasks, respectively. Latent substance use included six indicators of use of cigarettes, marijuana, beer, wine, liquor, and occasions of binge drinking with >4 drinks in a single setting. Multi-group analyses were also conducted, with the same CLPMs separated into constrained groups for boys/men and girls/women. In addition, main analyses included change score regression analyses using arithmetic change scores, subtracting time 1 substance use from time 2 substance use, and subtracting time 1 from time 2 neural activity for each ROI per task. Change scores were also calculated for time 2 to time 3 substance use, and time 1 to time 3 substance use. Analyses included both past 3 months substance use (to capture recent use) and past 2 years substance use (to capture longer-term use), to compare effects between recent use and the possibility of more occasional use. Observed variables included neural responses to monetary reward anticipation and social inclusion in the bilateral NAcc and bilateral mPFC, and covariates of gender, age, previous substance use, and depression recruitment status.

Results

Preliminary Analyses

Descriptive statistics for all study variables across time 1/age 17, time 2/age 19, and time 3/age 21 are presented in Table 2.2. Average substance use (both past 3 months and past 2 years) was relatively low at time 1, increased by time 2, and then increased substantially by time 3 when most participants (89%) were of legal age. Results from neuroimaging ROI analyses with the contrast Gain Anticipation > Neutral Anticipation for MID and Social Inclusion > Baseline for Cyberball are shown in Figure 2.6, and corresponding *t*-values and peak coordinates are shown in Table 2.3. Social inclusion during Cyberball elicited significant activity in the NAcc (Figure 2.6C) and mPFC (Figure 2.6D) at both time points. Further, Figure 2.7 displays the patterns of neural activation for each participant at time 1 and time 2 within each ROI per task.

These plots suggest more variability in mPFC response to social inclusion (Figure 2.7D) than NAcc response to inclusion (Figure 2.7C), NAcc response to monetary reward (Figure 2.7A), and mPFC response to monetary reward (Figure 2.7B). Variability in mPFC response to social inclusion appeared to be similar between time 1 and time 2.

Table 2.4 presents bivariate correlations among study variables at each time point. Associations were positive and significant between ROIs within each task (e.g., NAcc and mPFC response to monetary reward at time 1), suggesting that the mPFC was responsive to both types of reward in a similar fashion as the NAcc (Table 2.4). Between the two types of rewards, however, time 1 mPFC response to monetary reward was negatively correlated with time 1 mPFC response to social reward; thus, the mPFC could serve different functions depending on whether the reward is social in nature or not. Additionally, activity was not significantly correlated within the ROIs and task across time (e.g., NAcc response to monetary reward at time 1 was not significantly correlated with NAcc to monetary reward at time 2), indicating either low stability over time or significant developmental change between the ages of 17 and 19 on average. Simple regressions confirmed some of these findings while controlling for gender and previous substance use; for example, time 1 mPFC activity while anticipating monetary reward was associated with NAcc activity within the same task, $\beta = .16$, $t_{119} = 1.97$, $p = .041$; and NAcc activity to social reward at time 1 was related to mPFC activity within the same task, $\beta = .31$, $t_{119} = 6.76$, $p < .001$. Time 1 mPFC activity was also related between monetary and social reward, but negatively, $\beta = -.11$, $t_{119} = -2.12$, $p = .035$. There were no significant zero-order correlations between ROIs and substance use measures.

Table 2.5 displays bivariate correlations involving change scores. NAcc response to monetary reward at time 1 was positively associated with change in mPFC response to monetary

reward from time 1 to time 2 (Table 2.5); similarly, mPFC response to monetary reward at time 1 was positively correlated with change in NAcc response to monetary reward over time. NAcc response to social reward at times 1 and 2 was associated with change in mPFC response to social reward, and mPFC response to social reward at time 1 was negatively associated with change in NAcc to social reward. Greater change in NAcc response to monetary reward was associated with greater change in mPFC response to reward, and the same result was found for change in social reward. There were no significant zero-order correlations between ROI change scores and substance use measures.

A series of t-tests were conducted to examine changes in study variables over time. NAcc response to monetary reward decreased from time 1 to time 2 (t_{119} = 2.90, two-sided p = .004, 95% CI [.02 – .10]), whereas mPFC response did not change significantly (t_{119} = -1.11, two-sided p = .26, 95% CI [-.05 – .02]). mPFC activity during social inclusion increased from time 1 to time 2 (t_{119} = -2.23, two-sided p = .02, 95% CI [-.16 – -.01]); and NAcc activity remained similar between time points (t_{119} = 1.37, two-sided p = .17, 95% CI [-.02 – .09]). When examining L and R hemispheres separately, the patterns remained similar, suggesting no hemispheric differences in change in activity. For example, left NAcc response to monetary reward decreased significantly (t_{119} = 2.95, two-sided p = .004, 95% CI [.03 – .13]), along with right NAcc response (t_{119} = 2.63, two-sided p = .01, 95% CI [.02 – .13]). Response to monetary reward did not change over time for the left mPFC (t_{119} = -1.43, two-sided p = .19, 95% CI [-.07 – .01]) or the right mPFC (t_{119} = -1.10, two-sided p = .28, 95% CI [-.07 – .02]). Left mPFC activity during social reward increased significantly (t_{119} = -2.29, two-sided p = .02, 95% CI [-.15 – -.01]), as did right mPFC activity (t_{119} = -2.07, two-sided p = .03, 95% CI [-.14 – -.01]). Left NAcc activity during social reward did not change significantly (t_{119} = 1.12, two-sided p =

.28, 95% CI [-.02 – .03]), nor did right NAcc activity during social reward (t_{119} = 1.45, two-sided p = .15, 95% CI [-.02 – .05]).

Regarding composite scores for substance use, the sum of use overall in the past 3 months did not change significantly from time 1 to time 2 (t_{119} = -1.57, two-sided p = .11, 95% CI [-1.05 – .11]). Substance use sum during the past 3 months increased from time 2 to time 3 (t_{119} = -5.56, two-sided p < .001, 95% CI [-2.89 – -1.37]), and from time 1 to time 3 (t_{119} = -7.78, two-sided p < .001, 95% CI [-3.26 – -1.93]). Substance use sum during the past 2 years increased from time 1 to time 2 (t_{119} = -4.79, two-sided p < .001, 95% CI [-.73 – -.30]), from time 2 to time 3 (t_{119} = -4.08, two-sided p < .001, 95% CI [-1.01 – -.35]), and from time 1 to time 3 (t_{119} = -6.52, two-sided p < .001, 95% CI [-1.56 – -.83]).

Table 2.2

Descriptive Statistics for Study Variables

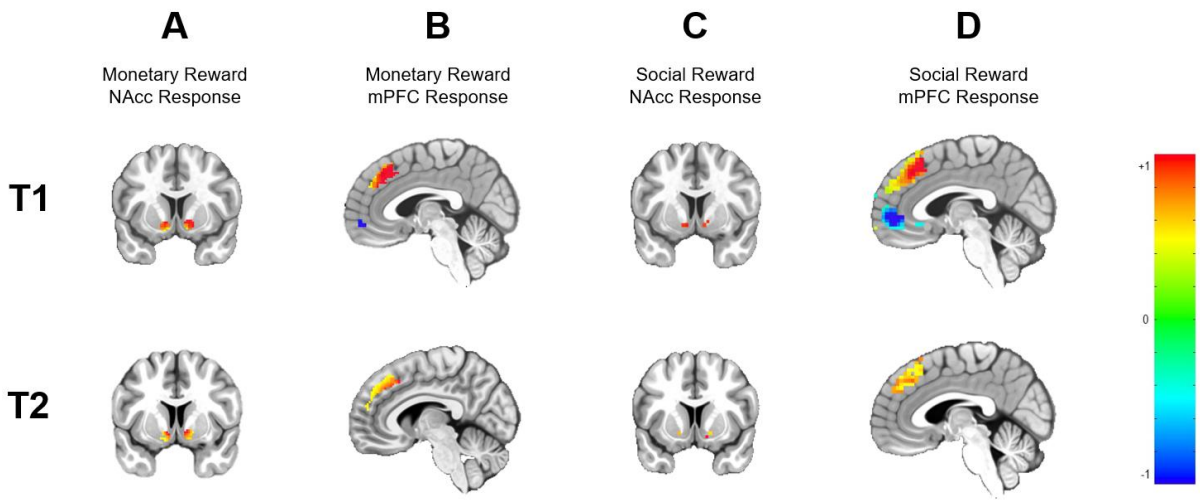
	Time 1	Time 2	Time 3
Variable	*M (SD)*	*M (SD)*	*M (SD)*
NAcc Response to Monetary Reward	.18 (.13)	.11 (.22)	
mPFC Response to Monetary Reward	.00 (.15)	.02 (.14)	
NAcc Response to Social Reward	.01 (.17)	-.02 (.24)	
mPFC Response to Social Reward	-.06 (.29)	.02 (.33)	
Substance Use in Past 3 Months (Sum)	.92 (2.12)	1.38 (2.51)	3.57 (3.72)
Substance Use in Past 2 Years (Sum)	1.71 (1.98)	2.29 (1.71)	3.33 (1.84)
Substance Use Before Age 14 (Covariate)	N_{Yes} = 42		
	N_{No} = 78		
Age at Time of MRI Scan	17.22 (.44)	19.19 (.44)	
Previous Substance Use	.43 (.50)		
Depression Recruitment Status	.87 (.34)		
Change in NAcc Response to Monetary Reward from T1		-.06 (.24)	
Change in mPFC Response to Monetary Reward from T1		.02 (.21)	
Change in NAcc Response to Social Reward from T1		-.03 (.28)	
Change in mPFC Response to Social Reward from T1		.09 (.42)	
Change in Sum Substance Use from T1 (Past 3 Months)		.47 (3.24)	
Change in Sum Substance Use from T1 (Past 2 Years)		.52 (1.18)	
Change in Sum Substance Use T2 to T3 (Past 3 Months)			2.18 (4.38)
Change in Sum Substance Use T2 to T3 (Past 2 Years)			.68 (1.83)
Change in Sum Substance Use T1 to T3 (Past 3 Months)			2.65 (3.81)
Change in Sum Substance Use T1 to T3 (Past 2 Years)			1.20 (2.02)

Note: *N* = 120. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, *M* = Mean, *SD* = Standard deviation. Time 1/T1 refers to the first study visit when participants were approximately 17 years old, Time 2/T2 refers to the second visit when participants were approximately 19 years old, and Time 3/T3 refers to the third visit when participants were approximately 21 years old. Monetary Reward refers to neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task. Social Reward refers to neural response in the contrast Inclusion > Baseline in the Cyberball task. Substance use in Past 3 Months refers to ratings on past 3 months use on a scale of Never (0) to Almost Every Day (4), summing across 6 substance types: cigarettes, cannabis, beer, wine, liquor, and binge drinking. Past 2 Years refers to use since the previous time point with response options of No (0) or Yes (1). Previous Substance Use is a covariate to control for early substance use, created as a dichotomous variable with Never (0) and At Least Once (1). Depression Recruitment Status is

coded as Low (0) and Elevated (1), and it represents the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV, and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire. Change scores are arithmetic.

Figure 2.6

Contrast Maps from Region-of-Interest Analyses of Monetary and Social Rewards



Note: *N* = 120. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, T1 = Time 1 first study visit when participants were approximately 17 years old, T2 = Time 2 second visit when participants were approximately 19 years old. Monetary Reward refers to neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task. Social Reward refers to neural response in the contrast Social Inclusion > Baseline in the Cyberball task. Activity is shown for NAcc Response to Monetary Reward (Panel A), mPFC Response to Monetary Reward (Panel B), NAcc Response to Social Reward (Panel C), and mPFC Response to Social Reward (Panel D).

Table 2.3

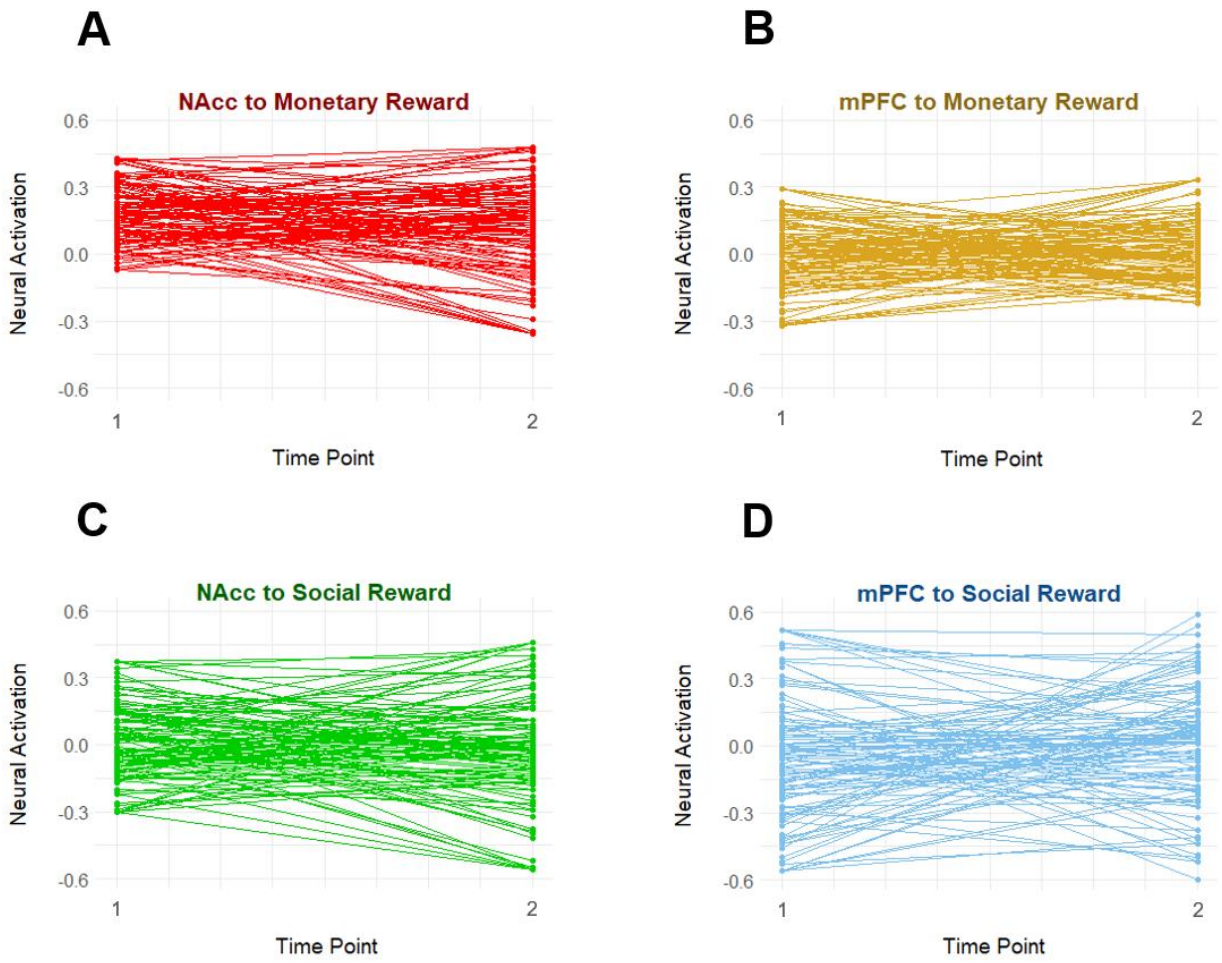
T-statistics and Peak Coordinates from Region-of-Interest Analyses of Monetary and Social Rewards

		Time 1				Time 2			
		Statistic	Peak Coordinates (MNI)			Statistic	Peak Coordinates (MNI)		
Task	Region	*t*	x	y	z	*t*	x	y	z
MID	L NAcc	9.47*	-16	4	-14	7.88*	-11	6	-13
	R NAcc	9.54*	18	6	-12	6.89*	13	5	-12
	L mPFC	4.95*	-3	15	44	3.98*	-2	20	45
	R mPFC	4.92*	2	16	42	4.02*	1	18	42
Cyberball	L NAcc	3.92*	-16	10	-9	2.91*	-14	10	-8
	R NAcc	3.11*	12	11	-11	3.11*	12	9	-10
	L mPFC	4.65*	-5	24	39	4.67*	-7	22	37
	R mPFC	4.49*	4	18	43	4.72*	5	19	40

Note. $N = 120$. * indicates p-corrected < .05. MID = Monetary Incentive Delay task for neural response to monetary reward, R = Right hemisphere, L = Left hemisphere, NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, MNI = Montreal Neurological Institute stereotaxic space. x, y, and z = MNI coordinates in the left–right, anterior–posterior, and inferior–superior dimensions, respectively. t = t-score for the contrast of interest at the given coordinates (local maxima), with a minimum threshold $t = 2.575$, $p < .05$ corrected for each search region. Time 1 refers to the first study visit when participants were approximately 17 years old, and Time 2 refers to second visit when participants were approximately 19 years old.

Figure 2.7

Change in Neural Responses to Monetary and Social Rewards



Note: *N* = 120. NAcc = Nucleus accumbens, and mPFC = Medial prefrontal cortex. Time 1 refers to the first study visit when participants were approximately 17 years old, and Time 2 refers to the second visit when participants were approximately 19 years old. Monetary Reward refers to neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task. Social Reward refers to neural response in the contrast Inclusion > Baseline in the Cyberball task.

Table 2.4

Bivariate Correlations among Study Variables

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. Gender	1																
2. Age	.05	1															
3. Depression Recruitment Status	-.11	.02	1														
4. Previous Substance Use	-.14	.18*	.15	1													
5. NAcc Monetary Reward T1	.15†	-.14	.05	.17†	1												
6. mPFC Monetary Reward T1	.09	-.11	.10	.01	.20*	1											
7. NAcc Monetary Reward T2	.02	.12	.15†	-.02	.09	.01	1										
8. mPFC Monetary Reward T2	-.03	-.13	.04	-.08	-.05	-.09	.35**	1									
9. NAcc Social Reward T1	.02	.04	.10	-.17†	-.11	-.07	.00	.10	1								
10. mPFC Social Reward T1	-.04	.02	.00	-.12	-.09	-.21*	-.02	.03	.54**	1							
11. NAcc Social Reward T2	-.10	-.08	-.08	.03	-.10	.00	-.02	.03	.09	.16†	1						
12. mPFC Social Reward T2	-.03	-.10	-.09	-.08	-.05	.03	-.13	-.07	.06	.09	.52**	1					
13. SU Past 3 Months T1	.03	.03	.01	-.01	.01	.12	-.07	.05	-.03	-.01	.00	.05	1				
14. SU Past 2 Years T1	.00	.01	.02	-.13	-.03	.11	.03	.07	-.02	-.01	.08	.06	.64**	1			
15. SU Past 3 Months T2	.07	.02	-.01	-.07	-.04	.14	-.05	-.02	.08	.03	-.13	.07	.03	-.01	1		
16. SU Past 2 Years T2	-.01	.01	.01	.01	.04	.09	.02	.10	.01	.00	.10	.05	.54**	.78**	.09	1	
17. SU Past 3 Months T3	.05	.01	.09	.17†	-.06	.14	.12	-.01	.04	-.03	.10	.04	.23*	.32**	.06	.30**	1
18. SU Past 2 Years T3	-.10	.09	.11	.14	-.12	.14	.01	.04	.01	-.05	.08	.08	.28**	.38**	.02	.47**	.69**

Note: $N = 120$. $^{\dagger}p < 0.10$, $*p < 0.05$; $**p < 0.01$; $***p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, Monetary Reward = Monetary reward from neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, Social Reward = Social reward from neural response in the contrast Social Inclusion > Baseline in the Cyberball task, SU = Substance use sum score across 6 types, T1 = Time 1 first study visit when participants were approximately 17 years old, T2 = Time 2 second visit when participants were approximately 19 years old, and T3 = Time 3 third visit when participants were approximately 21 years old. Gender is coded as 0 = Girls/Women, 1 = Boys/Men.

Table 2.5

Bivariate Correlations among Study Variables and Change Scores

	Change in NAcc Monetary Reward	Change in mPFC Monetary Reward	Change in NAcc Social Reward	Change in mPFC Social Reward	Change in SU Past 3 Months T1-T2	Change in SU Past 2 Years T1-T2	Change in SU Past 3 Months T2-T3	Change in SU Past 2 Years T2-T3	Change in SU Past 3 Months T1-T3	Change in SU Past 2 Years T1-T3
Gender	-.06	-.09	-.10	.00	.03	-.01	.02	.07	.04	-.09
Age	.01	.02	.00	.04	.00	.02	.02	.12	.02	.08
Depression Recruitment Status	.11	-.04	-.12	-.07	-.01	-.01	.08	-.08	.08	.08
Previous Substance Use	-.10	-.06	.13	.02	-.05	.20*	.17†	-.11	.16†	.24**
NAcc Monetary Reward T1	-.46**	-.17†	-.02	.02	-.04	.11	-.03	-.16†	-.07	-.08
mPFC Monetary Reward T1	-.10	-.74**	.04	.17†	.03	-.04	.04	.06	.06	.04
NAcc Monetary Reward T2	.84**	.22*	-.02	-.09	.01	-.02	.12	-.01	.15†	-.02
mPFC Monetary Reward T2	.34**	.73**	-.03	-.08	-.05	.04	.00	-.06	-.04	-.03
NAcc Social Reward T1	.06	.12	-.52**	-.32**	.10†	.05	-.01	.00	.10†	.03
mPFC Social Reward T1	.03	.16†	-.17*	-.61**	.03	.02	-.05	-.05	-.03	-.04
NAcc Social Reward T2	.03	.03	.80**	.29**	-.10	.04	.16†	-.02	.10	.01
mPFC Social Reward T2	-.09	-.07	.40**	.72**	.03	-.02	-.02	.04	.00	.02
SU Past 3 Months T1	-.06	-.04	.02	.05	-.63**	-.20*	.18*	-.21*	-.32**	-.31**
SU Past 2 Years T1	.05	-.03	.08	.06	-.42**	-.38**	.25**	-.33**	-.07	-.53**
SU Past 3 Months T2	-.02	-.11	-.16†	.04	.75**	.14	-.53**	-.06	.03	.03
SU Past 2 Years T2	-.01	.01	.08	.04	-.27**	.29**	.19*	-.46**	-.02	-.24**
SU Past 3 Months T3	.13	-.10	.07	.05	-.11	-.03	.80**	.41**	.83**	.36**
SU Past 2 Years T3	.07	-.07	.06	.10	-.16†	.11	.55**	.57**	.50**	.58**

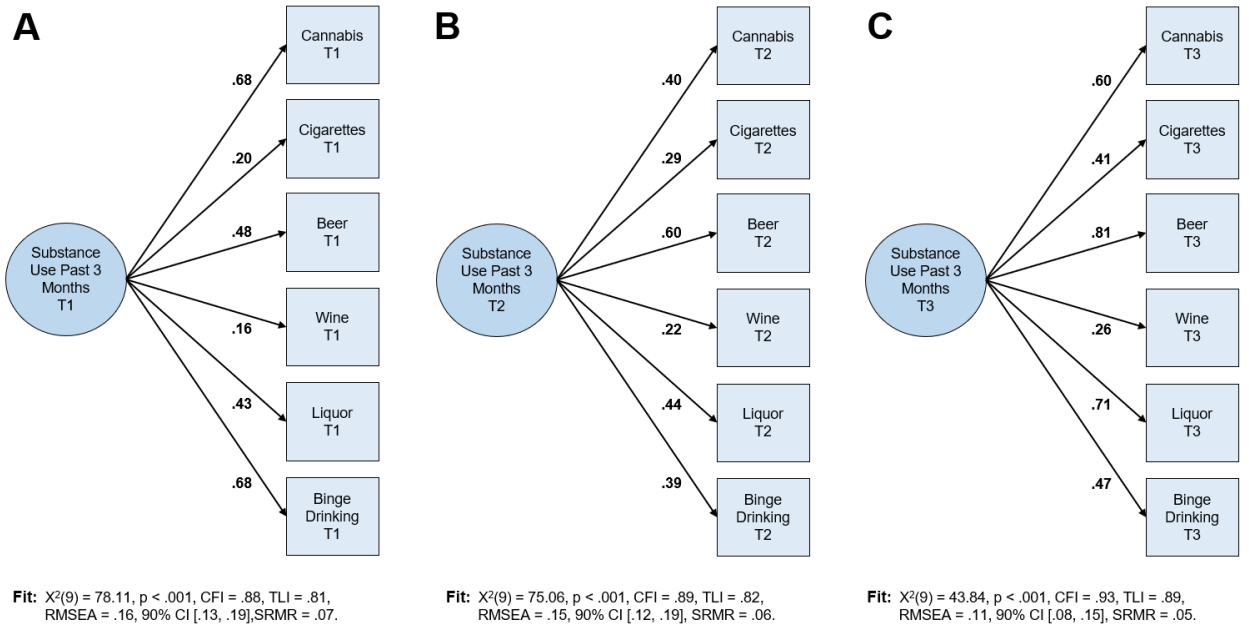
Note: $N = 120$. $^{\dagger}p < 0.10$, $*p < 0.05$; $**p < 0.01$; $***p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, Monetary Reward = Monetary reward from neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, Social Reward = Social reward from neural response in the contrast Inclusion > Baseline in the Cyberball task, SU = Substance use sum score across 6 types, T1 = Time 1 first study visit when participants were approximately 17 years old, T2 = Time 2 second visit when participants were approximately 19 years old, and T3 = Time 3 third visit when participants were approximately 21 years old. Changes scores are arithmetic.

Measurement Models

Latent factor structure for substance use at times 1, 2, and 3 was tested with six confirmatory factor analyses, including three for past 3 months use and three for past 2 years use. Model fit was considered excellent if: CFI ≥ 0.90, TLI ≥ 0.90, RMSEA ≤ 0.08, and SRMR ≤ 0.08 (Hu & Bentler, 1999; Kline, 2023). For past 3 months use, goodness-of-fit was adequate except for RMSEA values for all time points (standardized estimates presented): time 1 (Figure 2.8A), time 2 (Figure 2.8B), and time 3 (Figure 2.8C). For past 2 years use, fit was good for time 1 (Figure 2.9A), and adequate except for RMSEA values for time 2 (Figure 2.9B) and time 3 (Figure 2.9C). Removing use of cigarettes and/or wine only slightly improved the fit of models.

Figure 2.8

Confirmatory Factor Analysis of Substance Use (Past 3 Months)

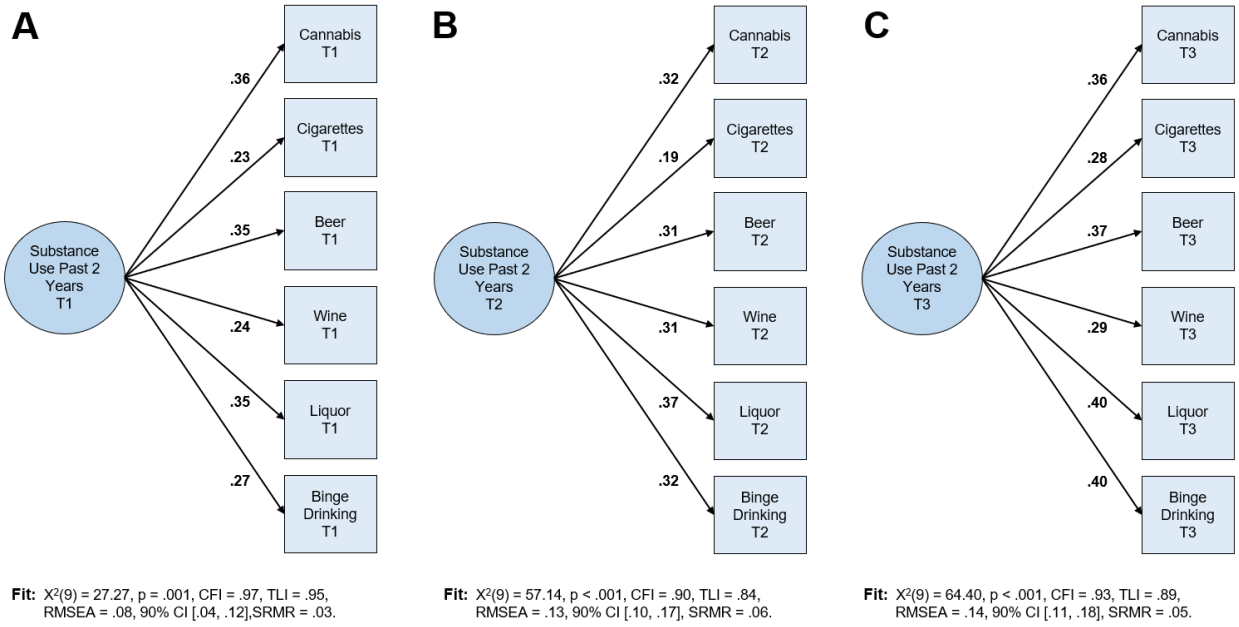


Note: X^2 = chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = confidence interval, and SRMR = Standardized root mean square residual. Standardized estimates presented. Substance use during the past 3 months reflects using the substance at least once per month during the past 3 months.

Panel A shows Time 1 when participants were approximately 17 years old, Panel B shows Time 2 when participants were approximately 19 years old, and Panel C shows Time 3 when participants were approximately 21 years old.

Figure 2.9

Confirmatory Factor Analysis of Substance Use (Past 2 Years)



Note: X^2 = chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = confidence interval, and SRMR = Standardized root mean square residual. Standardized estimates presented. Substance Use Past 2 Years refers to use since the previous time point with response options of No (0) or Yes (1). T1 = Time 1 (A) when participants were approximately 16 years old, T2 = Time 2 (B) when participants were approximately 19 years old, and T3 = Time 3 (C) when participants were approximately 21 years old.

Next, the results of cross-lagged panel models (CLPMs) and change score regression analyses are presented below. Sections are separated into past 3 months substance use and past 2 years use. All analyses included control variables gender (coded as "0 = *Women*"), age at the time of the first MRI scan, previous substance use before age 14 (coded as "0 = *Never tried any substance*" or "1 = *Tried at least one substance on at least one occasion*"), and depression recruitment status (coded as "0 = *Low risk for depression*" or "1 = *Elevated risk for depression*").

Substance Use in Past 3 Months

Cross-Lagged Panel Model

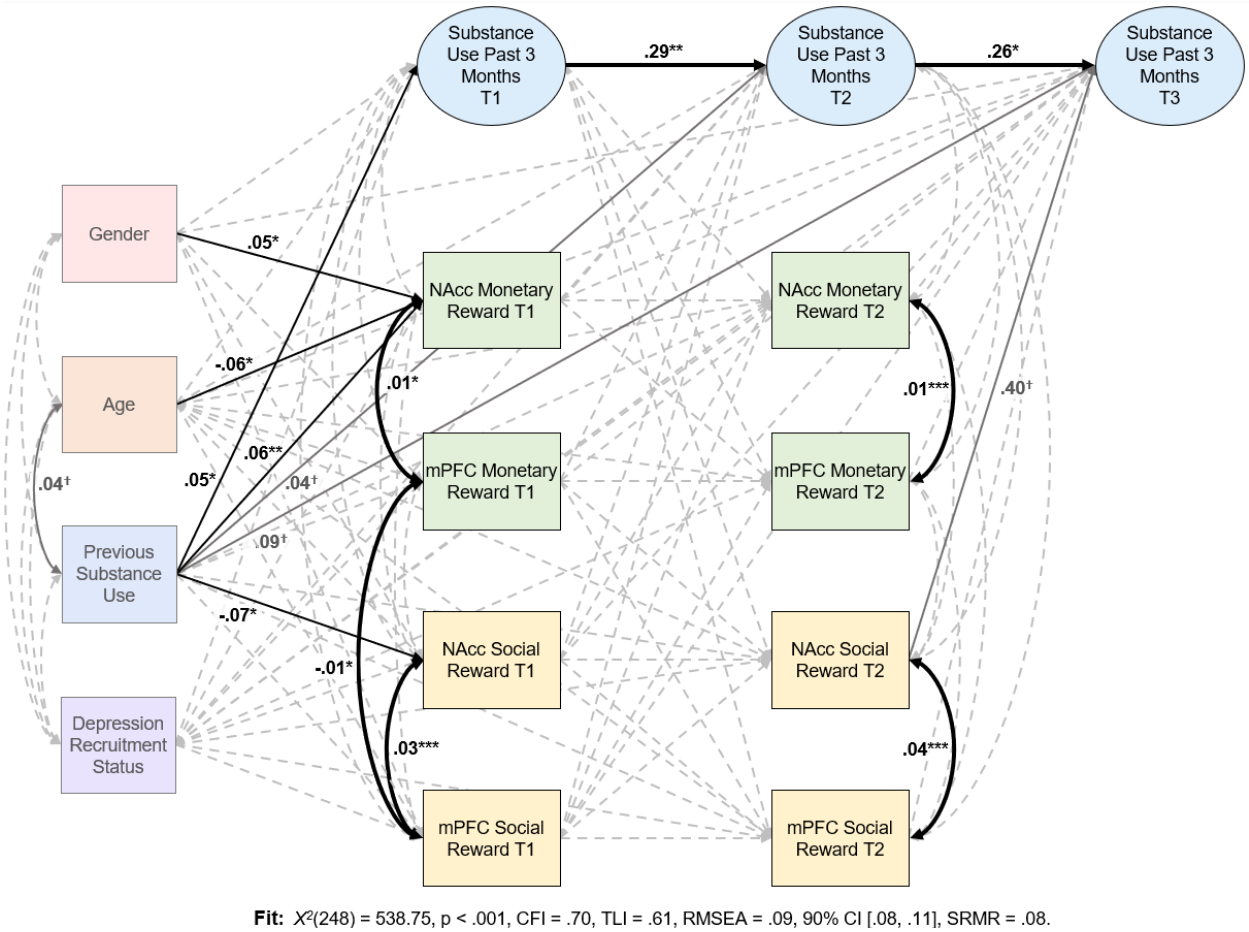
In the CLPM with neural activity for the two ROIs for each task at time 1 and time 2 and latent past 3 months substance use across time 1/age 17, time 2/age 19, and time 3/age 21, model fit was poor (Figure 2.10). Time 1 substance use predicted time 2 use, and time 2 use predicted time 3 use. Previous substance use by age 14 was positively associated with time 1 use, but not later use. Previous use was also positively associated with NAcc activity while anticipating monetary reward, whereas it was negatively associated with NAcc activity while receiving social reward. Boys demonstrated greater NAcc response to monetary reward at time 1, as did younger adolescents overall. NAcc activity to monetary reward was positively associated with mPFC activity to monetary reward, at both time 1 and time 2. Neural activity to social reward in the NAcc and the mPFC was also positively related at times 1 and 2. Across tasks, however, higher mPFC activity to monetary reward at time 1 was associated with lower mPFC activity to social reward. This pattern was specific to time 1 and not observed during time 2. Neural activity at time 1 did not significantly predict activity at time 2, or substance use during young adulthood.

To further examine the association between gender and NAcc response to monetary reward at time 1, an exploratory multi-group SEM analysis was conducted with separate groups for men and women (Figure 2.11). In the model including women, NAcc response to monetary reward increased from time 1 to time 2, and substance use did not change significantly from time 2 to time 3. Age was negatively associated with NAcc response to monetary reward. Previous substance use predicted substance use at time 1, but no other study variables. The association between NAcc and mPFC response to monetary reward at time 1 was not significant. In the model including men, NAcc response to monetary reward was positively associated with NAcc

response to social reward. Previous substance use predicted more NAcc response to monetary reward, but did not significantly predict NAcc response to social reward. Age was not significantly associated with other study variables, and NAcc response to monetary reward was not associated with mPFC response to monetary reward. Thus, there were gender differences in the associations between the two reward types at time 1, and in the stability/change in responses within regions and tasks over time; and only younger girls showed less NAcc activity while anticipating reward, as the association between age and NAcc response was negative for girls.

Figure 2.10

Cross-Lagged Panel Model with Substance Use (Past 3 Months) and Neural Responses to Monetary and Social Rewards

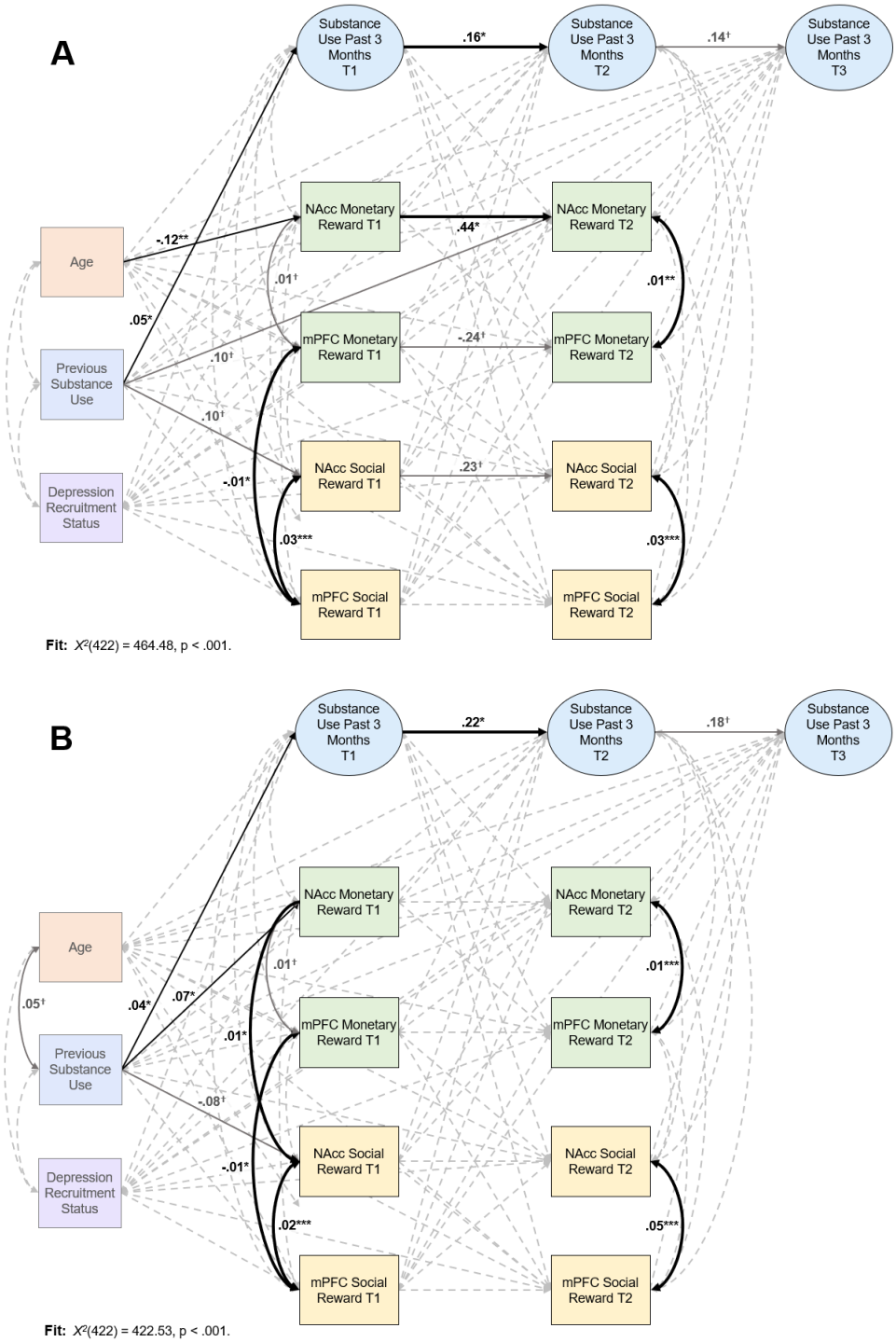


Note: $N = 120$. $^{\dagger}p < 0.10$, $*p < 0.05$; $**p < 0.01$; $***p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, T3 = Time 3 when participants were approximately 21 years old, Substance Use = Latent substance use with indicators marijuana, cigarettes, beer, liquor, and binge drinking, X^2 = chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = confidence interval, and SRMR = Standardized root mean square residual. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Social Inclusion > Baseline in the Cyberball task. Gender is coded as 0 = Women, 1 = Men. Previous Substance Use is a covariate representing early substance use before age 14, coded as Never = 0 and At Least Once = 1. Depression Recruitment Status is a covariate coded as 0 = Low and 1 = Elevated, and it represents the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview

Schedule for Children-IV, and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire. Value in parentheses is degrees of freedom for the chi-square model. Dashed lines represent nonsignificant paths; solid lines represent significant or marginal paths. Indicators of latent factors omitted for visual clarity.

Figure 2.11

Multi-Group Analysis of Path Coefficients between Women and Men for Substance Use (Past 3 Months) and Neural Responses to Monetary and Social Rewards



Note: n = 62 for Women (A) and n = 58 for Men (B). $p < 0.10$, *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, T3 = Time 3 when participants were approximately 21 years old, Substance Use = Latent substance use with indicators marijuana, cigarettes, beer, liquor, and binge drinking, and X^2 = chi-square goodness-of-fit. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Social Inclusion > Baseline in the Cyberball task. Previous Substance Use is a covariate representing early substance use before age 14, coded as Never = 0 and At Least Once = 1. Depression Recruitment Status is a covariate coded as 0 = Low and 1 = Elevated, and it represents the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV, and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire. Value in parentheses is degrees of freedom for the chi-square model. Dashed lines represent nonsignificant paths; solid lines represent significant or marginal paths. Indicators of latent factors omitted for visual clarity.

Change Score Regressions

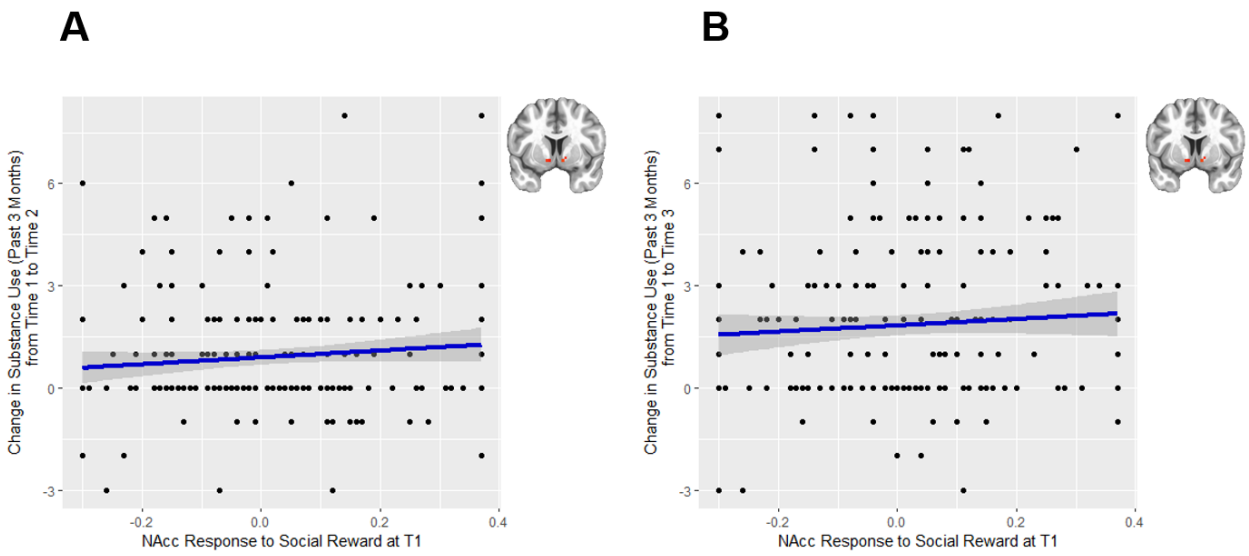
To address hypotheses involving rate of change in neural activity and substance use over time, a series of regression analyses were conducted with arithmetic change scores. Response to social reward in the NAcc at time 1 predicted change in substance use during the past three months from time 1 to time 2, such that higher NAcc activity in mid-adolescence was associated with an increase in substance use into young adulthood, as shown in Figure 2.12A and Table 2.6. Over a longer timespan from time 1 to time 3, NAcc response at time 1 predicted more change in past 3 months substance use (Figure 2.12B). Activity in the mPFC during social inclusion at time 1 was not significantly associated with change in substance use, nor was activity in the NAcc or mPFC while anticipating monetary reward (Table 2.6). Taken together, greater activity to social reward in the NAcc during mid-adolescence was associated with a steeper increase in substance use (past 3 months) by age 18; but this pattern was not found for mPFC activity, or for activity to monetary (i.e., non-social) reward. Regarding past 3 months substance use at time 1 and change in neural activation, results of these analyses were not statistically significant (see supplementary materials in Appendix B). These associations included time 1 substance use and change in NAcc response to monetary reward (Table B1 in Appendix B), mPFC and monetary reward (Table B2 in Appendix B), NAcc and social reward (Table B3 in Appendix B), and mPFC and social reward (Table B4 in Appendix B).

When examining rate of change in neural activity as it relates to rate of change in substance use together, greater change in NAcc response to monetary reward was related to greater change in substance use from time 1 to time 3, as shown in Figure 2.13 and Table 2.6. In other words, individuals for whom there were greater increases in NAcc activity while anticipating monetary reward from 17 to 19 years were likely to report greater increases in

substance use from 16 to 21 years. This result contrasts with the finding that higher NAcc response to social reward at time 1 predicted more change in substance use, whereas change in NAcc response to social reward did not significantly predict change in substance use from adolescence to young adulthood.

Figure 2.12

Regression with Neural Response to Social Reward Predicting Change in Substance Use (Past 3 Months)



Note: *N* = 120. NAcc = Nucleus accumbens, Time 1 occurred when participants were approximately 17 years old, Time 2 occurred when participants were approximately 19 years old, and Time 3 occurred when participants were approximately 21 years old. Social Reward represents neural response in the contrast Social Inclusion > Baseline in the Cyberball task. Associations were significant at *p*-corrected < .05. Change scores were arithmetic. Panel A represents change in substance use (past 3 months) from Time 1 to Time 2, and Panel B represents change in substance use (past 3 months) from Time 1 to Time 3.

Table 2.6

Regression with Neural Responses to Monetary and Social Rewards Predicting Change in Substance Use (Past 3 Months)

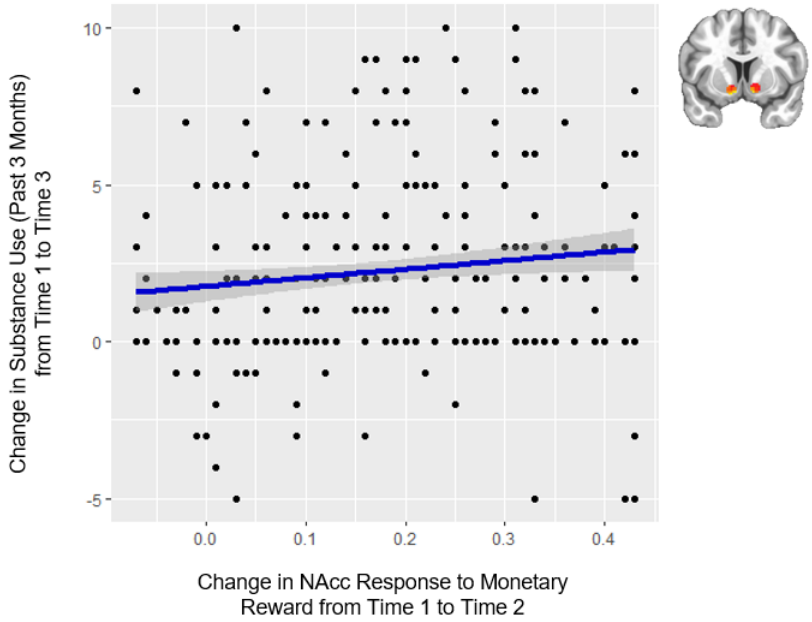
Outcome	Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	Fit
Change in Use T1-T2	(Intercept)	.52	[-.31, 1.35]				
	NAcc Monetary	-.39	[-3.72, 2.95]	-.02	[-.17, .13]	.00	
	mPFC Monetary	1.23	[-1.88, 4.35]	.06	[-.09, .21]	.00	
	NAcc Social	3.41*	[.19, 6.62]	.18	[.01, .35]	.02	
	mPFC Social	-.43	[-2.36, 1.50]	-.04	[-.21, .13]	.00	
	Gender	.25	[-.66, 1.15]	.04	[-.10, .18]	.00	
	Age	.04	[-1.55, 1.63]	.01	[-.19, .20]	.00	
	Previous Substance Use	.16	[-1.43, 1.12]	.02	[-.22, .17]	.00	
	Depression Recruitment Status	-.15	[-1.97, 1.67]	-.02	[-.21, .18]	.00	
							R^2 = .032 95% CI [.00,.07]
	(Intercept)	.38	[-1.56, 2.17]				
	Change NAcc Monetary	.72	[-.47, 1.24]	.05	[-.14, .25]	.00	
	Change mPFC Monetary	-.99	[-3.95, 1.97]	-.07	[-.26, .13]	.00	
	Change NAcc Social	-1.95	[-4.34, .43]	-.17	[-.37, .04]	.02	
	Change mPFC Social	.54	[-1.05, 2.14]	.07	[-.14, .28]	.00	
	Gender	.08	[-1.12, 1.27]	.01	[-.17, .20]	.00	
	Age	-.10	[-1.69, 1.49]	-.01	[-.21, .18]	.00	
	Previous Substance Use	.14	[-1.38, 1.11]	.02	[-.21, .17]	.00	
	Depression Recruitment Status	-.31	[-2.13, 1.50]	-.03	[-.22, .16]	.00	
							R^2 = .028 95% CI [.00,.07]
Change in Use T2-T3	(Intercept)	1.47**	[.38, 2.56]				
	NAcc Monetary	1.02	[-3.38, 5.43]	.04	[-.12, .19]	.00	
	mPFC Monetary	.02	[-4.08, 4.13]	.00	[-.15, .15]	.00	
	NAcc Social	.35	[-3.89, 4.58]	.01	[-.16, .19]	.00	
	mPFC Social	-1.44	[-3.99, 1.10]	-.10	[-.27, .07]	.01	
	Gender	-.43	[-1.63, .76]	-.05	[-.19, .09]	.00	
	Age	-.37	[-2.49, 1.74]	-.03	[-.23, .16]	.00	
	Previous Substance Use	1.63†	[-.07, 3.33]	.18	[-.01, .38]	.03	
	Depression Recruitment Status	.71	[-1.72, 3.14]	.06	[-.13, .24]	.00	
							R^2 = .011 95% CI [.00,.03]
	(Intercept)	2.37**	[1.22, 3.52]				
	Change NAcc Monetary	2.58	[-.87, 6.04]	.14	[-.05, .33]	.02	
	Change mPFC Monetary	-1.29	[-5.26, 2.69]	-.06	[-.26, .13]	.00	
	Change NAcc Social	2.68†	[-.52, 5.88]	.17	[-.03, .37]	.02	
	Change mPFC Social	-.63	[-2.77, 1.52]	-.06	[-.27, .15]	.00	
	Gender	.33	[-1.28, 1.93]	.04	[-.15, .22]	.00	
	Age	-.47	[-2.57, 1.63]	-.04	[-.23, .15]	.00	
	Previous Substance Use	1.46†	[-.18, 3.11]	.17	[-.02, .35]	.03	
	Depression Recruitment Status	.76	[-1.64, 3.16]	.06	[-.13, .25]	.00	
							R^2 = .043 95% CI [.00,.09]
Change in Use T1-T3	(Intercept)	1.99**	[1.07, 2.92]				
	NAcc Monetary	.64	[-3.08, 4.36]	.03	[-.12, .18]	.00	
	mPFC Monetary	1.26	[-2.22, 4.73]	.05	[-.10, .20]	.00	
	NAcc Social	3.75*	[.17, 7.34]	.18	[.01, .35]	.02	
	mPFC Social	-1.87†	[-4.03, .28]	-.15	[-.32, .02]	.01	
	Gender	-.19	[-1.20, .82]	-.03	[-.17, .11]	.00	
	Age	-.33	[-2.15, 1.49]	-.03	[-.23, .16]	.00	
	Previous Substance Use	1.47*	[.01, 2.94]	.19	[.00, .38]	.03	
	Depression Recruitment Status	.56	[-1.53, 2.65	.05	[-.14, .24]	.00	
							R^2 = .028 95% CI [.00,.06]

(Intercept)	2.75*	[1.75, 3.75]			
Change NAcc Monetary	3.31*	[.31, 6.30]	.21	[.02, .40]	.04
Change mPFC Monetary	-2.28	[-5.73, 1.16]	-.13	[-.32, .06]	.01
Change NAcc Social	.73	[-2.05, 3.50]	.05	[-.15, .26]	.00
Change mPFC Social	-.08	[-1.94, 1.77]	-.01	[-.21, .20]	.00
Gender	.40	[-.99, 1.79]	.05	[-.13, .24]	.00
Age	-.57	[-2.39, 1.25]	-.06	[-.25, .13]	.00
Previous Substance Use 14	1.33†	[-.10, 2.75]	.17	[-.01, .36]	.03
Depression Recruitment Status	.45	[-1.63, 2.53]	.04	[-.15, .23]	.00
					R^2 = .049
					95% CI [.00,.10]

Note: N = 120. Corrected $^{\dagger}p < 0.10$, $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, *b* = Unstandardized regression weights, *beta* = Standardized regression weights, sr^2 = Semi-partial correlation squared, CI = Confidence interval, *LL* and *UL* = Lower and upper limits of a confidence interval, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, and T3 = Time 3 when participants were approximately 21 years old. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Social Inclusion > Baseline in the Cyberball task. Change scores were arithmetic. Gender is coded as 0 = Women, 1 = Men. Previous Substance Use is a covariate representing early substance use before age 14, coded as Never = 0 and At Least Once = 1. Depression Recruitment Status is a covariate coded as 0 = Low and 1 = Elevated, and it represents the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV, and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire. A significant *b*-weight indicates the beta-weight and semi-partial correlation are also significant.

Figure 2.13

Regression for Change in NAcc Response to Social Reward Predicting Change in Substance Use (Past 3 Months)



Note: N = 120. NAcc = Nucleus accumbens, Time 1 occurred when participants were approximately 17 years old, Time 2 occurred when participants were approximately 19 years old, and Time 3 occurred when participants were approximately 21 years old. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task. Associations were significant at p-corrected < .05. Change scores were arithmetic.

Substance Use in Past 2 Years

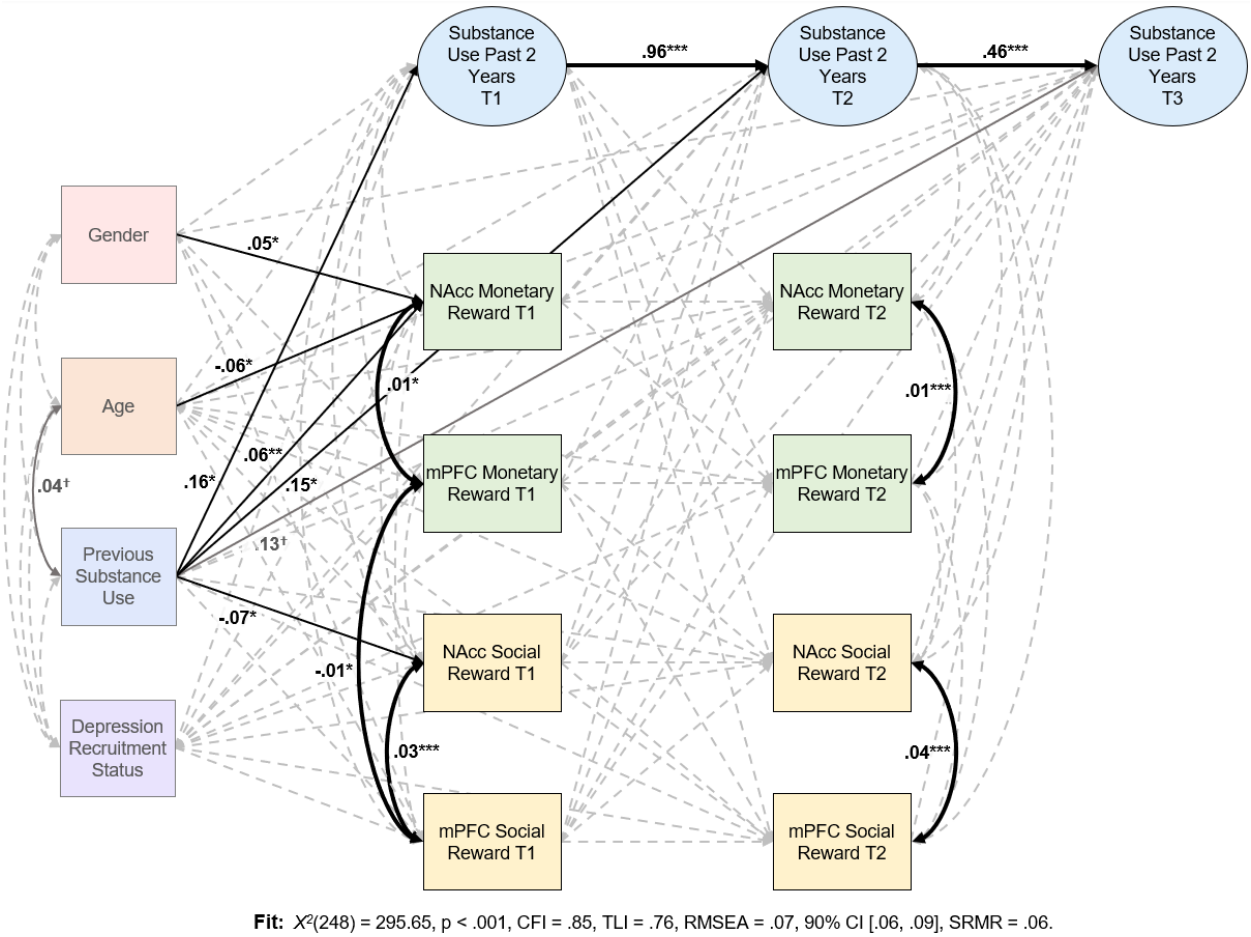
Cross-Lagged Panel Model

Model fit for the CLPM involving substance use in the past 2 years was better than that of use in the past 3 months (Figure 2.14), and results were largely similar. Time 1 substance use predicted time 2 substance use, and time 2 use predicted time 3 use. Previous substance use by age 14 predicted later use at time 1 and time 2. Thus, it is possible that experimenting with substances farther in the past (i.e., longer than 3 months before the study visits) during adolescence does not necessarily mean that young adults will endorse higher use at age 21.

In the multi-group analysis (Figure 2.15), adolescent girls' early substance use predicted more use by time 1 and time 2; and their substance use at time 2 predicted use at time 3. The findings about time 2 substance use were different from the previous multi-group analysis with past-3-months' use, but other coefficients were similar. Boys' early substance use predicted greater use at times 1, 2, and 3; and time 2 use predicted time 3 use. Although early substance use did not predict time 3 use in women, this effect was significant in men. The findings about substance use at time 2 and time 3 were different from the previous multi-group analysis with past-3-months' use.

Figure 2.14

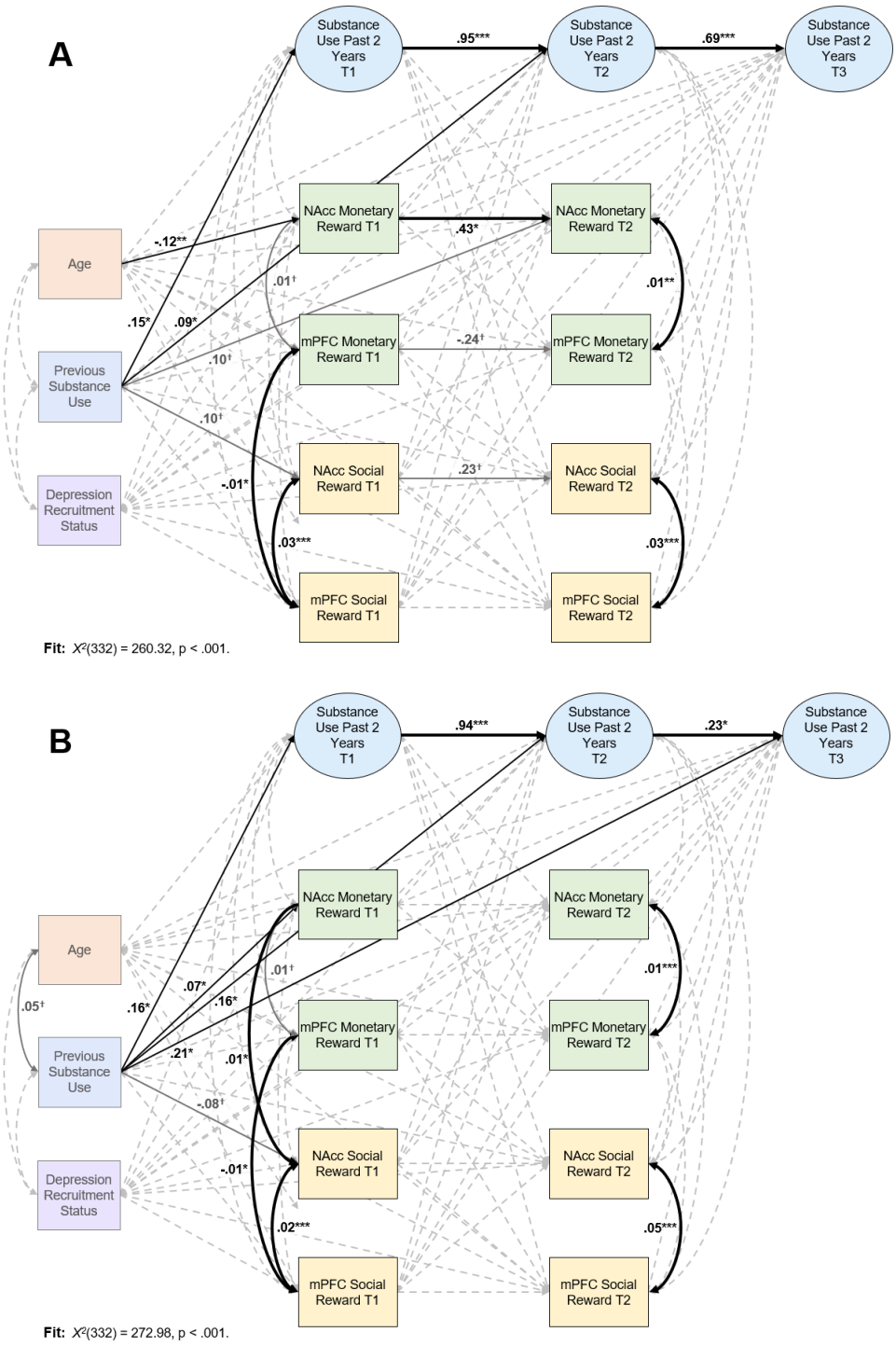
Cross-Lagged Panel Model with Substance Use (Past 2 Years) and Neural Responses to Monetary and Social Rewards



Note: $N = 120$. $^{\dagger}p < 0.10$, $*p < 0.05$; $**p < 0.01$; $***p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, T3 = Time 3 when participants were approximately 21 years old, Substance use = Latent substance use with indicators marijuana, cigarettes, beer, and liquor, X^2 = chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = confidence interval, and SRMR = Standardized root mean square residual. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Social Inclusion > Baseline in the Cyberball task. Gender is coded as 0 = Women, 1 = Men. Value in parentheses is degrees of freedom for the chi-square model. Dashed lines represent nonsignificant paths; solid lines represent significant or marginal paths. Indicators of latent factors omitted for visual clarity.

Figure 2.15

Multi-Group Analysis of Path Coefficients between Women and Men for Substance Use (Past 2 Years) and Neural Responses to Monetary and Social Rewards



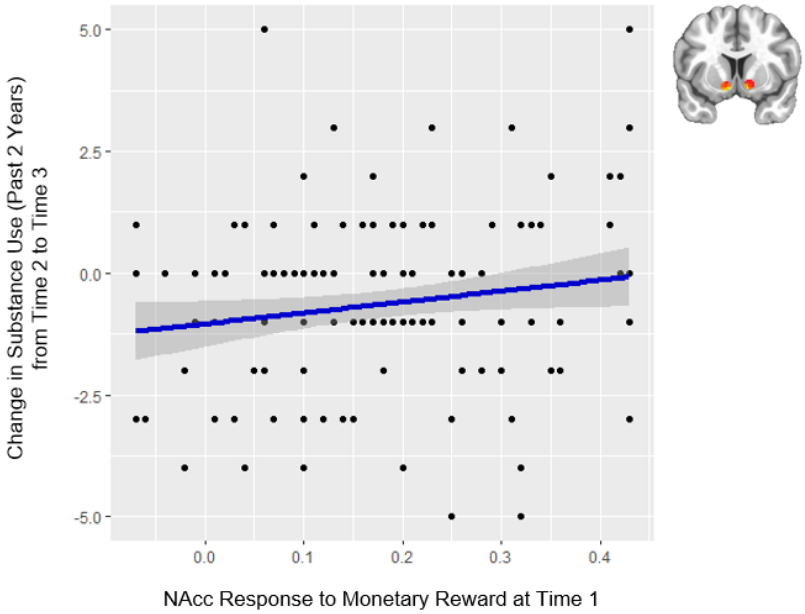
Note: n = 62 for Women (A) and n = 58 for Men (B). $p < 0.10$, *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, T3 = Time 3 when participants were approximately 21 years old, Substance Use = Latent substance use with indicators marijuana, cigarettes, beer, and liquor, and X^2 = chi-square goodness-of-fit. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Social Inclusion > Baseline in the Cyberball task. Previous Substance Use is a covariate representing early substance use before age 14, coded as Never = 0 and At Least Once = 1. Depression Recruitment Status is a covariate coded as 0 = Low and 1 = Elevated, and it represents the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV, and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire. Value in parentheses is degrees of freedom for the chi-square model. Dashed lines represent nonsignificant paths; solid lines represent significant or marginal paths. Indicators of latent factors omitted for visual clarity.

Change Score Regressions

Greater neural response to monetary reward at time 1 predicted more change in substance use during the past 2 years from time 2 to time 3 (Figure 2.16). Other associations were not statistically significant (Table 2.7). Change in substance use was not significantly associated with change in neural activity over time for monetary reward and NAcc (Table B5 in Appendix B) or mPFC (Table B6 in Appendix B), nor for social reward and NAcc (Table B7 in Appendix B) or mPFC (Table B8 in Appendix B). Thus, neural activity appears to be more predictive of change in recent use during the past 3 months, compared to change in use during the past 2 years.

Figure 2.16

Regression with Neural Response to Monetary Reward Predicting Change in Substance Use (Past 2 Years)



Note: *N* = 120. NAcc = Nucleus accumbens, Time 1 occurred when participants were approximately 17 years old, Time 2 occurred when participants were approximately 19 years old, and Time 3 occurred when participants were approximately 21 years old. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task. Associations were significant at *p*-corrected < .05. Change scores were arithmetic.

Table 2.7

Regression with Neural Responses to Monetary and Social Rewards Predicting Change in Substance Use (Past 2 Years)

Outcome	Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	Fit
Change in Substance Use T1-T2	(Intercept)	.36*	[.01, .71]				
	NAcc Monetary	1.31†	[-.09, 2.71]	.14	[-.01, .29]	.02	
	mPFC Monetary	.32	[-.98, 1.63]	.04	[-.11, .19]	.00	
	NAcc Social	.40	[-.94, 1.75]	.05	[-.12, .22]	.00	
	mPFC Social	-.22	[-1.02, .59]	-.05	[-.21, .12]	.00	
	Gender	-.18	[-.56, .20]	-.07	[-.21, .07]	.00	
	Age	-.06	[-.62, .51]	-.02	[-.21, .17]		
	Previous Substance Use	.50*	[.05, .95]	.21	[.02, .40]	.04	
	Depression Recruitment Status	-.20	[-.85, .45]	.06	[-.25, .13	.00	
							R^2 = .027 95% CI [.00,.06]
	(Intercept)	.50**	[.18, .81]				
	Change NAcc Monetary	-.49	[-1.44, .45]	-.10	[-.29, .09]	.01	
	Change mPFC Monetary	.42	[-.66, 1.51]	.08	[-.12, .27]	.01	
	Change NAcc Social	.06	[-.82, .94]	.01	[-.19, .22]	.00	
	Change mPFC Social	-.08	[-.66, .51]	-.03	[-.24, .18]	.00	
	Gender	-.03	[-.47, .41]	-.01	[-.20, .17]	.00	
	Age	-.04	[-.61, .53]	-.01	[-.21, .18]	.00	
	Previous Substance Use	.49*	[.05, .94]	.21	[.02, .40]	.04	
	Depression Recruitment Status	-.13	[-.78, .53]	-.04	[-.23, .15]	.00	
							R^2 = .012 95% CI [.00,.02]
Change in Substance Use T2-T3	(Intercept)	1.21**					
	NAcc Monetary	2.84*	[.15, 5.31]	.20	[.01, .39]	.04	
	mPFC Monetary	1.16	[-.10, .28]	.09	[-.02, .04]	.01	
	NAcc Social	.24	[-.19, .24]	.02	[-.01, .01]	.00	
	mPFC Social	-.38	[-.28, .16]	-.06	[-.01, .02]	.00	
	Gender	-.27	[-.26, .11]	-.07	[-.02, .03]	.01	
	Age	.84†	[-.02, 1.70]	.18	[-.00, .37]	.03	
	Previous Substance Use	.55	[-.15, 1.25]	.15	[-.04, .34]	.02	
	Depression Recruitment Status	.35	[-.65, 1.35]	.07	[-.12, .25]	.00	
							R^2 = .042 95% CI [.00,.09]
	(Intercept)	.88**	[.40, 1.37]				
	Change NAcc Monetary	.87	[-.59, 2.32]	.11	[-.08, .31]	.01	
	Change mPFC Monetary	-.98	[-2.65, .70]	-.11	[-.31, .08]	.01	
	Change NAcc Social	-.44	[-1.79, .91]	-.07	[-.27, .14]	.00	
	Change mPFC Social	.37	[-.53, 1.27]	.08	[-.12, .29]	.01	
	Gender	-.36	[-1.03, .32]	-.10	[-.28, .09]	.01	
	Age	.84†	[-.04, 1.72]	.18	[-.01, .37]	.03	
	Previous Substance Use	.48	[-.21, 1.18]	.13	[-.06, .32]	.02	
	Depression Recruitment Status	.25	[-.77, 1.26]	.05	[-.14, .24]	.00	
							R^2 = .033 95% CI [.00,.08]
Change in Substance Use T1-T3	(Intercept)	1.31**	[.79, 1.83]				
	NAcc Monetary	.08	[-2.03, 2.19]	.01	[-.14, .16]	.00	
	mPFC Monetary	.48	[-1.49, 2.45]	.04	[-.11, .19]	.00	
	NAcc Social	.59	[-1.44, 2.62]	.05	[-.12, .22]	.00	
	mPFC Social	-.52	[-1.74, .70]	-.07	[-.24, .10]	.00	
	Gender	-.64*	[-1.21, -.07]	-.16	[-.30, -.02]	.02	
	Age	-.80†	[-1.73, .13]	-.16	[-.35, .03]	.02	
	Previous Substance Use	1.05**	[.29, 1.82]	.26	[.07, .45]	.06	

Depression Recruitment Status	.15	[-.94, 1.25]	.03	[-.16, .21]	.00	
						R^2 = .027
						95% CI [.00,.06]
(Intercept)	1.38**	[.85, 1.92]				
Change NAcc Monetary	.37	[-1.24, 1.98]	.04	[-.15, .24]	.00	
Change mPFC Monetary	-.55	[-2.40, 1.30]	-.06	[-.25, .14]	.00	
Change NAcc Social	-.38	[-1.87, 1.11]	-.05	[-.26, .15]	.00	
Change mPFC Social	.29	[-.71, 1.29]	.06	[-.15, .27]	.00	
Gender	-.38	[-1.13, .36]	-.10	[-.28, .09]	.01	
Age	-.76†	[-1.71, .19]	-.15	[-.34, .04]	.02	
Previous Substance Use	.98*	[.22, 1.74]	.24	[.05, .43]	.05	
Depression Recruitment Status	.12	[-.99, 1.22]	.02	[-.17, .21]	.00	
						R^2 = .016
						95% CI [.00,.03]

Note: N = 120. Corrected $^{\dagger}p < 0.10$, $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, *b* = Unstandardized regression weights, *beta* = Standardized regression weights, sr^2 = Semi-partial correlation squared, CI = Confidence interval, *LL* and *UL* = Lower and upper limits of a confidence interval, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, and T3 = Time 3 when participants were approximately 21 years old. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Inclusion > Baseline in the Cyberball task. A significant *b*-weight indicates the beta-weight and semi-partial correlation are also significant. Change scores were arithmetic. Gender is coded as 0 = Women, 1 = Men.

Discussion

The present longitudinal study investigated how neural responses to social and non-social rewards were associated with substance use reciprocally over time from adolescence to young adulthood, and how change in neural responses was related to change in substance use. This study is the first to include, in the same model, neural responses in specific reward-related brain regions to both types of rewards at two timepoints; and the first to examine their associations with substance use longitudinally. Results expand upon previous research by comprehensively assessing substance use, conceptualizing use as both latent and observed, and as both recent (during the past 3 months) and within a longer time frame (during the past 2 years). Additionally, this work contextualizes different neurodevelopmental theories by incorporating concepts of adolescent risk-taking, social attunement, testing bidirectional connections over time, and informing how these complex processes might occur in non-WEIRD populations as the study involved individuals who are Mexican-origin. Hypotheses regarding neural activity included that (1) social inclusion during Cyberball (i.e., social reward) would elicit activity in the NAcc and mPFC, and this activity will be positively associated with that of monetary reward, (2) NAcc response to reward will be positively associated with mPFC response to reward within each task, (3) this activity would decrease from ages 17 to 19, (4) neural activity while anticipating monetary reward would also decrease. Regarding substance use, hypotheses included that (5) more neural response to both rewards would be associated with more substance use concurrently, (6) greater neural activity would predict more substance use prospectively through age 21, (7) more neural response to inclusion at ages 17 and 19 would predict more change in substance use by ages 18 and 21, respectively, such that higher social reward response would lead to a steeper increase in use, and (8) change in social reward response would predict change in substance use,

such that adolescents with a steeper decrease in NAcc/mPFC response (i.e., more change) would increase in substance use more gradually (i.e., less change). Additionally, an exploratory hypothesis about gender was that (9) boys with greater NAcc response to monetary reward might show increased substance use, whereas girls with greater mPFC response might show increased substance use; but no directional predictions were made about gender differences in neural response to social reward. These hypotheses were partially supported.

First, social reward versus a neutral baseline elicited greater neural activity in the NAcc and mPFC – two key regions implicated in reward processing and impulse control – at both ages 17 and 19. Areas of peak activation to social reward occurred within similar coordinates as found in monetary reward, and with similar magnitude for mPFC response, but with lower values for NAcc response to social reward. In the same manner, the ROI contrast maps showed visual similarities between mPFC activation to monetary and social reward, but differences for NAcc activation as social reward appeared to result in weaker activation. Regarding associations among regions and tasks, responses to social inclusion were positively correlated between the NAcc and mPFC, within each time point. Activity in these regions was also correlated within the monetary reward task. An exploratory multi-group analysis found that, among boys, NAcc responses were positively associated between monetary and social rewards at age 17; and this effect was not found in girls. The lack of an association between NAcc response to both types of rewards in the overall sample suggests that gender differences are key, as explained later in this section. This study is the first to explore how neural response to social reward is related to neural response to monetary reward in a sample of adolescents. Among young adults, Jarcho et al. (2022) found that more severe substance use behavior was associated with higher right VS

response to monetary reward, and lower right VS response to social reward. The two types of reward, however, were not directly compared to each other.

Surprisingly, mPFC responses across the two tasks at age 17 were negatively associated, such that adolescents with higher mPFC response to social reward demonstrated lower response to monetary reward. This finding was unexpected, and the small literature thus far about mPFC activity to social and non-social rewards prevents drawing strong conclusions. Still, one possibility is that this effect is driven by greater variability in social reward response across the mPFC, as contrast maps and intraindividual change plots suggested that social reward elicited a larger area of activation in dorsal areas of the mPFC (compared to monetary reward) but also a larger area of deactivation in more ventral areas of the mPFC. Future analyses could address the role of neighboring regions by separating out activation of the vmPFC and dmPFC, to test if there is a positive association between tasks for the dmPFC and a negative association for the vmPFC. Examining mPFC response to social reward over time also suggested high variability, in both activity within each time point and in change in activity. For example, some adolescents began with low mPFC response to social inclusion that then increased by age 19, whereas others began with high mPFC response that then decreased over time. Variability was higher for this region than for the NAcc. Prior studies have reported associations between substance use and activity during social reward in the VS (Flannery et al., 2023; Jarcho et al., 2022), but have not examined the role of the mPFC. Flannery et al. (2023) found that social reward via the Social Incentive Delay (SID) task activated the VS in adolescents, and Jarcho et al. (2022) found that peer acceptance activated the VS in young adults. In both of those studies, the VS mask was defined by the Harvard-Oxford Structural Atlas and included areas beyond the NAcc alone. The current study's finding that social inclusion activated the NAcc aligns with prior work, but as the

existing literature is limited, more work is needed to better understand the role of the mPFC, despite the mPFC being implicated in response to monetary reward (e.g., Swartz et al., 2020).

Second, NAcc activity while anticipating monetary reward decreased from age 17 to age 19 in regression analyses, in line with expectations that reward response would decrease. However, it was also found that mPFC activation to social reward increased, and no significant changes emerged for mPFC response to monetary reward or NAcc response to social reward. Another unexpected finding was that, among girls only in the multi-group analyses, NAcc response to monetary reward increased over time; and boys showed no significant change in this activity. Thus, the finding that change was observed in simple regressions but not cross-lagged models with the overall sample suggests that gender differences could play an important role. These patterns are interesting, especially given the relatively small window of time between scans (approximately two years). Previous longitudinal work with the MID has found that striatal activation while anticipating high gain (contrasted with low gain) increased between the ages of 16 and 20 (Lamm et al., 2014). Using a gambling task with younger adolescents, however, van Duijvenvoorde et al. (2014) reported no significant change in VS response between the ages of 13 and 16; and Baranger et al. (2021) found trait-like stability in neural responses during a card-guessing task between the ages of 15 and 22. Regarding social reward, only one study has tested longitudinal changes in neural activation, revealing a quadratic effect in which VS response to social inclusion in Cyberball was high around age 7, decreased around age 11, and then increased by age 14 (van der Meulen et al., 2023). More work is needed to elucidate these patterns in older adolescents and young adults, as well as how changes in activation coincide with changes in substance use. In the current study, substance use overall increased from age 18 to age 21, as expected given the normative increase as individuals reach legal drinking age in the

U.S. (Miech et al., 2024). Substance use during the past 3 months did not vary substantially between the ages of 16 and 18, although substance use during the past 2 years was higher at age 18, indicating more occasional use overall. Substance use levels and rate of change were only somewhat associated with neural response to either type of reward cue.

Third, higher reward-related neural activity during social inclusion at age 17 was associated with a greater increase in substance use from ages 16 to 18, suggesting that greater activity may indicate greater sensitivity to being included by others, and that sensitivity increases adolescents' risk of using more substances within the next two years. This finding appears to be unidirectional, as age 16 substance use did not predict change in neural activation by age 19. When considering a broader time frame, NAcc response to social reward at age 17 also predicted change in substance use from age 16 to age 21, but not from age 18 to age 21. This pattern might indicate that the link between social reward neural activity and substance use is unique to adolescence, and subsides by young adulthood. This interpretation is in line with the social plasticity hypothesis of substance use desistance during young adulthood (Cousijn et al., 2017), in which greater social attunement (e.g., being more tuned in to changing social norms around substance use) supports decreases in use into adulthood. Heightened NAcc response predicting more substance use supports the impulsivity theory of addiction (Buckholtz et al., 2010; Luijten et al., 2017), whereas the lack of an association at age 21 also supports the social plasticity model (Cousijn et al., 2017). One explanation is that individuals who are more sensitive (neurally) to social experiences are more likely to use substances to fit in with friends and other peers during adolescence, but less likely to use substances to fit in with others who decrease in their use during adulthood. To test this possibility further, future research could examine change in substance use over time in both social and non-social contexts; for example, surveys could ask

adolescents how often they drink alcohol alone and how often they drink with peers. fMRI tasks could also probe social and non-social substance-related stimuli, as was done by Groefsema et al. (2020) in a study of adults' alcohol use after viewing alcohol-related cues that were either social or non-social in nature. Another interesting future direction would be to explore cultural values unique to this sample of Mexican-origin adolescents, such as familism (a traditional value centered on family closeness and obligation), which can serve as a social protective factor from substance use (Lardier et al., 2018). Mexican-American adolescents could be highly committed to their peers in a similar way that they are dedicated to their family. Future work could also compare neural response to social inclusion by both peers and family members, and measure associations with self-reported peer and family closeness as they relate to substance use.

Fourth, greater change in NAcc response to monetary (i.e., non-social) reward from 17 to 19 was associated with greater change in substance use from age 16 to age 21, but not from ages 16 to 18 or from ages 18 to 21. In other words, adolescents who increased in NAcc activity while anticipating monetary gain by age 19 were more likely to increase their consumption of substances by age 21, compared to those who decreased or experienced no change in their response to monetary reward. This effect, however, only occurred in the broad five-year interval and was not found in the shorter intervals from ages 16 to 18 and ages 18 to 21. It is possible that higher motivation to receive monetary reward during the transition to young adulthood results in individuals also being more motivated to try new substances, or to use them more frequently than they did during adolescence. The link between change in neural response and change in substance use was specific to the NAcc, and not found in the mPFC; and it was specific to monetary reward. Increases in reward-related activity being linked to increases in substance use supports the impulsivity theory of addiction (Buckholtz et al., 2010; Luijten et al., 2017).

Fifth, change in social reward response was not related to change in substance use, contrary to predictions. In previous work, Flannery et al. (2023) found that substance-using adolescents showed increased VS activity to social reward over time, whereas non-using adolescents did not show change. Contrary to these results but with a cross-sectional design, Jarcho et al. (2022) found that VS response to positive peer feedback was negatively associated with substance use among young adults. Thus, it is difficult to establish if heightened or blunted striatal response to social reward is a risk factor for later substance use. Incorporating a third wave of fMRI data collection at age 21 would have allowed comparisons of change in substance use with change in brain activity from ages 17 to 21. In addition, a larger sample would allow comparisons between adolescents who regularly use substances and those who do not.

History of early substance use before the age of 14 was included as a covariate and not a main variable of interest, but two interesting patterns emerged between early use and later neural activity in response to rewards. Adolescents who had endorsed previous substance use demonstrated greater NAcc activation during monetary reward at age 17, suggesting that early use might sensitize adolescents to be motivated to seek out financial incentives. Conversely, adolescents with previous substance use showed less NAcc activation during social reward, suggesting that early use can lead to blunted striatal response to social rewards in particular. Although these associations were between early use before age 14 and neural responses at age 17, the pattern is consistent with what Jarcho and colleagus (2022) found among young adults. Problematic substance use behaviors were related with greater right VS response to monetary reward, but lower right VS response to social reward. Future work is needed to highlight how differential profiles of hypo- and hyper-activation to different types of rewards might be a consequence of early substance use, and/or a risk factor for future substance use.

Finally, the current study revealed gender-specific pathways for change in NAcc activity while anticipating monetary reward, and how a history of early substance use might shape this activity. During adolescence, boys showed greater NAcc response to monetary reward at age 17 in the cross-lagged models. A multi-group analysis suggested that boys who reported using substances by age 14 demonstrated greater NAcc response to monetary reward at age 17, and this NAcc activity was positively associated with NAcc response to social reward, a pattern not found among girls or in the full sample. The positive association between boys' substance use and NAcc response to monetary reward is similar to results found by Swartz et al. (2020), in which boys with greater NAcc activity while anticipating monetary reward increased in alcohol use later on. Conversely, girls' NAcc response to monetary reward increased over time (whereas there was a decrease in the full sample found in simple regressions), and girls who were younger at time 1 (age 17) responded more strongly to monetary reward in the NAcc, two effects not found among boys. The cross-lagged association between NAcc response to monetary reward at each time point in the full sample could have been washed out by the lack of a significant effect in boys. Early substance use, however, was not associated with neural activity among girls. Swartz et al. (2020) reported that girls with low NAcc and high dmPFC activity to monetary reward increased in later alcohol use. The current study did not find any links among mPFC response and substance use, in girls or boys, although future work should disentangle activity in the ventral and dorsal regions of the mPFC. Thus, there might be gender-specific associations between NAcc activity in the two types of reward, and in stability or change in activation over time; but mPFC activity might follow a different pattern, or not be significantly associated with early substance use. Future work should confirm these pathways in a larger sample, as the current analyses were limited to 62 women and 58 men.

Differences in substance use have been reported across racial and ethnic groups. Risk for heavy substance use is higher for Latinx populations than for White populations, and Mexican-American individuals in particular tend to have an earlier onset of alcohol use (Atherton et al., 2016; Miech et al., 2024). The impact of social influences also varies; for example, Hispanic adolescents have been found to be less susceptible to influence from their friends' cigarette use than White adolescents (Unger et al., 2001). Although Mexican-American adolescents are vulnerable to substance use, cultural assets also offer protection. As one example, greater endorsement of familism is typically associated with less substance use (e.g., Ma et al., 2016). Latinx populations are also under-represented in developmental neuroscience work. In one study, Mexican-American adolescents who reported higher familism demonstrated lower VS response to monetary reward, as well as higher response in the dlPFC (Telzer et al., 2013). It is unknown whether this reduction in reward response would extend to social reward, and if it would influence substance use. Given the unique participants in the CFP, it would be interesting to examine the role of familism and other Mexican cultural values in the complex interplays of brain activation and substance use from adolescence to young adulthood.

The present study is not without limitations. First, a third wave of neuroimaging data would allow for other longitudinal analytic approaches such as latent growth curve modeling, and facilitate testing questions about change in brain activity across a wider age span within the context of change in substance use from ages 16 to 21. Nonetheless, the design of the present study afforded a novel opportunity to test change across two time points, as most previous work has been restricted to one occasion of neuroimaging. Another limitation of the present study is that the sample size, although large with 120 individuals, was restricted by a methodological change in the Cyberball task that prevented including an additional 40 participants. The MID

was administered during two substudies of the CFP, allowing for a combined sample; and Cyberball was also administered to those same participants, but with a change to task design and scan parameters due to needs of the second substudy. Additionally, the second time point of the substance use neurobiological substudy was limited by budget constraints, and included less individuals than the second time point of the depression neurobiological substudy. Testing associations in a larger sample size would have strengthened the ability to draw conclusions about change in neural activity and substance use over time. Third, another limitation is the conceptualization of monetary and social rewards. The anticipatory phase of the MID was selected due to its ability to capture motivation and its robust activation in previous literature (Bjork et al., 2008), but the feedback phase might be more appropriate to compare to social inclusion in Cyberball, which can be addressed in future work. Lastly, data were not collected about adolescents' social use of substances, such as behaviors within specific social situations or perceptions of friends' behaviors. Given that adolescents and young adults typically experiment with friends and other peers (Dishion & Tipsord, 2011), disentangling solitary and social use would provide additional insight. For example, an adolescent's responses might differ between questions about drinking alcohol alone versus drinking alcohol with friends or in other social situations. Relatedly, it would be interesting to compare Cyberball to other social reward tasks, such as the SID (Telzer et al., 2021) or those involving interactions with friends (Ambrosia et al., 2018; Flores et al., 2018), as well as assess adolescents' perceptions of the experience of social inclusion as a rewarding one. Future work could capture social aspects of substance use, and rely upon different tasks to probe neural activity while experiencing rewarding social situations.

In conclusion, the present study is the first to establish how the adolescent brain reacts to social and non-social rewards across time, and how these complex associations can partly

explain why some individuals consume more alcohol, cannabis, and tobacco as they enter young adulthood. Adolescence typically involves risky behaviors (Casey & Jones, 2010), and young adulthood involves a normative increase in substance use (Miech et al., 2024); however, substantial individual variability in these trajectories, as well as in brain development likely facilitates or constrains these patterns. Culture also contributes to variability in substance use, and this unique sample informs how reward-related brain activity maps onto substance use among adolescents of Mexican origin, a population under-studied in prior neuroscience research and vulnerable to problematic substance use.

In conclusion, this study found that (1) social inclusion reliably activates the NAcc and mPFC, (2) this reward-related activity changed over two years (age 17 to age 19), with mPFC response to social reward increasing (but NAcc not changing) and NAcc response to monetary reward decreasing (but mPFC not changing), (3) adolescents with more NAcc activity during social reward (but not monetary reward) showed a steeper increase in substance use by ages 18 and 21, and lastly, (4) adolescents whose response to monetary reward in the NAcc went up over time reported a steeper increase in substance use from age 16 to age 21 overall. Thus, individual variability in substance use from adolescence to young adulthood partially depends on how the developing brain processes potential monetary rewards and experienced social rewards. Despite limitations, these findings contribute new perspectives to theories about substance use such as the social plasticity hypothesis (Cousijn et al., 2017), and new insights into how the developing brain navigates social situations and makes decisions crucial to physical and mental health.

CHAPTER THREE

STUDY 2: SOCIAL EXPERIENCES AND SUBSTANCE USE FROM ADOLESCENCE TO YOUNG ADULTHOOD: THE ROLES OF NEURAL RESPONSE TO SOCIAL EXCLUSION AND RESISTANCE TO PEER INFLUENCE

Substance use is a significant public health problem that commonly onsets in adolescence and escalates in young adulthood (Miech et al., 2024). During adolescence, some experimenting is typical and unlikely to lead to long-term consequences; but earlier use is related to worse outcomes (Richmond-Rakerd et al., 2017), and heavy use can impact brain structure and function (Lees et al., 2020) and future social relationships (Clay & Parker, 2018). Substance use is more prevalent and severe among Latinx adolescents (Atherton et al., 2016; Trent et al., 2023). This disparity may stem from Latinx individuals' exposure to social stress, such as discrimination based on race (Vitoroulis & Georgiades, 2017); however, they may also benefit from cultural assets such as familism, a traditional Latinx value focused on family closeness and obligation (Lardier et al., 2018). Multiple factors have been identified that explain increases in substance use, but one domain particularly relevant during the developmental period of adolescence is social relationships (Brechwald & Prinstein, 2011; Dishion & Tipsord, 2011). Adolescents often begin using substances to conform to peers in social contexts (Bonar et al., 2022; Brechwald & Prinstein, 2011; Dishion & Tipsord, 2011), and/or to regulate negative affect (Conway et al., 2016; Felton et al., 2019; Hussong et al., 2011). Although peer influence has been implicated in risk-taking (Albert et al., 2013; Gardner & Steinberg, 2005; Smith et al., 2015), adolescents tend to avoid taking social risks that might lead to rejection (Do et al., 2016; Tomova et al., 2021). Individual differences in neurobiological sensitivity to social experiences, such as being excluded by peers, are crucial to identifying adolescents who may be at greater risk of problems.

Substance use typically declines throughout young adulthood into adulthood, due to a combination of social changes in responsibilities and maturation of brain regions supporting cognitive control and social cognition (Cousijn et al., 2017). In the Social Plasticity Hypothesis, Cousijn and colleagues (2017) suggested that neural and social mechanisms initially heighten the risk of excessive substance use during adolescence, but then lower the risk of continuation into adulthood and development of substance use disorders (SUDs). Social attunement, or the need to harmonize with the social environment, can motivate adolescents to engage in substance use to raise their social standing or fit into particular peer groups. As individuals progress into adulthood, being "attuned" to the social environment can result in the devaluation of substance use, as behaviors such as binge drinking (and associated consequences such as hangovers) are no longer perceived as socially desirable. Social attunement is supported by neural plasticity, or capacity for synaptic changes from environmental inputs, in networks involved in executive control, salience and attention, reinforcement learning, and social cognition. For example, adaptive behavioral changes can result from more mature functioning of associative learning mechanisms, mediated by the hippocampus (implicated in memory and learning), striatum (implicated in reward processing), dorsal anterior cingulate cortex (dACC, implicated in executive control), and the subgenual ACC and insula (both implicated in salience and attention). In addition, substance use risk can be lowered or heightened by specific social experiences.

Experiencing social stressors (e.g., peer victimization) during adolescence contributes to substance use in young adulthood, but substance use during adolescence may also impact later social functioning and neural processing of social stimuli during young adulthood. Substance use has been positively associated with experiencing peer victimization in general (Tretyak et al., 2022), ethnic-racial discrimination (Baiden et al., 2023), and problems in romantic relationships

(Larson & Sweeten, 2012), whereas use is negatively associated with support from family (S. Fisher et al., 2019) and some peers (Beard & Wolff, 2020; Coyle et al., 2016). Additionally, adults who heavily use substances struggle to maintain relationships (Clay & Parker, 2018; Sinha, 2008), and are more sensitive neurobiologically to the effects of social stress (Hanlon et al., 2018). At the same time, substance use impacts brain regions that support social cognition, further contributing to maladaptive social behavior (Cousijn et al., 2017; Sazhin et al., 2020). The current study tests how experiences of social support and social stress are bidirectionally associated with substance use from late childhood to young adulthood, and whether pathways are mediated by neural response to social exclusion and self-reported susceptibility to peers.

Adolescence is a developmental period characterized by more time spent with peers (Ashbourne & Daly, 2012) and a strong need for social acceptance with heightened sensitivity to social evaluation and potential social threats (Guyer & Jarcho, 2018; Nelson et al., 2016). Substance use during adolescence is highly social in nature, often occurring in social contexts (e.g., parties) and being highly influenced by perceptions of peers' behaviors (Dishion & Tipsord, 2011; Teunissen et al., 2012). Two of the biggest drivers of adolescents' substance use are having one or more friends who use substances (Branstetter et al., 2011; Pomrenze et al., 2022), and susceptibility to "peer pressure" from substance-using peers (Gallegos et al., 2021; Michael & Ben-Zur, 2007). These predictors also apply to young adults (Keyzers et al., 2020; Studer et al., 2014). Substance use has been linked to self-reported resistance to peer influence (RPI) (Monahan et al., 2009), as adolescents (Wojciechowski, 2023) and young adults (DiGuiseppi et al., 2018) who report less RPI (i.e., more susceptibility) are at a higher risk of problematic substance use. Peer relationships, however, can also provide positive support and discouragement of substance use (Beard & Wolff, 2020; Coyle et al., 2016; Farrell et al., 2017;

Han & Margolin, 2015). Indeed, peers represent an important source of both social support, and social stress (Michael & Ben-Zur, 2007). Despite the importance of social processes in substance use, few studies have investigated how neural processing of social events mediates the links between lived social experiences and substance use in adolescents and young adults.

Social Support and Substance Use

Social support can be conceptualized as the presence of a network of individuals that one can turn to in a time of need for emotional discussion, practical help, validation of self-worth, and/or sense of group membership (Cohen & Wills, 1985; Wills, 2004). Having supportive networks has been found to reduce substance use from adolescence to young adulthood (Ennett et al., 2008; Heerde & Hemphill, 2018; Woods-Jaeger et al., 2016). Latinx individuals might particularly benefit from social support, given the higher risk of experiencing stressors. Among young adults, peer support has also been negatively associated with substance use (Gliksberg et al., 2022; Stewart et al., 2023). Social support also reduces the impacts of adverse childhood experiences, such as physical abuse, on alcohol use in young adults (McCollum et al., 2023).

Most studies to date have assessed support from family and peers as one construct, but effects on substance use can differ by the source of support. Several studies have established that parental support is protective against substance use (Hummel et al., 2013; Mills et al., 2021; LaFreniere et al., 2021), including in racial/ethnic minority adolescents (Cruz et al., 2019; S. Fisher et al., 2019; Germãn et al., 2009; Woods-Jaeger et al., 2016). For example, Mills et al. (2021) found that adolescents who reported high levels of support from their parents were less likely to use alcohol and tobacco, and S. Fisher et al. (2019) found that multiracial adolescents with high parent support reported lower frequency of use of all substances. Strong endorsement of familism also predicts lower substance use in Hispanic adolescents (e.g., Lardier et al., 2018),

and mitigates the negative effects of affiliating with deviant peers (Germãn et al., 2009). Although parents continue to play a pivotal role during adolescence, the peer group is the most significant source of social support throughout this period (Michael & Ben-Zur, 2007); however, evidence about the direction of the association between peer support and substance use is mixed.

Some studies have reported that greater peer support led to higher levels of substance use (Gázquez et al., 2016; Lee et al., 2017; Piko, 2000), whereas others have found lower rates of substance use including in Hispanic and African-American youth (Forster et al., 2015), or no relation between peer support and substance use (Das et al., 2023). Among young adults, the literature is also mixed, with some work suggesting higher use (Cadigan et al., 2019; Studer et al., 2017) but other work suggesting lower use (Pauley & Hesse, 2009). The characteristics of peer groups are crucial, as receiving support from deviant peers (e.g., those engaging in substance use) heightens the risk of substance use, but receiving support from positive peers (e.g., those who disapprove of substance use and/or engage in prosocial behaviors) lowers the risk. Further, affiliating with positive peers has been identified as a protective factor against substance use (Coyle et al., 2015), and as a moderator that offsets substance use risk due to individual characteristics such as high sensation seeking (Beard & Wolff, 2020). Taken together, peer support can be protective against substance use, unless the source of support is peers who use substances or engage in other deviant behaviors.

Family and peer support also have interactive effects. For example, early negative family experiences such as parental derogation (e.g., having a parent who puts you down) predict lower social support in young adulthood (Gayman et al., 2011). A meta-analysis reported that supportive parent-adolescent relationships predicted supportive relationships with peers and romantic partners in young adulthood, while negative parent-adolescent relationships predicted

negative relationships (Schulz et al., 2023). Allen at al. (2012) found that having a close friend who uses substances predicted adolescents' substance use, but this effect was moderated by family experiences, such that adolescents were more likely to use substances if they felt less supported by their mothers. Another study revealed that high parental support predicted lower alcohol use during early adolescence, but this effect was mediated by their best friend's use of alcohol, only occurring among adolescents whose friends reported low or no use (LaFreniere et al., 2022). Social support can also buffer against adverse outcomes of being victimized by peers (Graber et al., 2016; Gunnar & Hostinar, 2015; Hansen et al., 2012; Wright, 2016).

Social Stress and Substance Use

Victimization by peers is a salient stressor that peaks during adolescence, as 40% of early adolescents report experiencing at least one instance of peer victimization at school (Catone et al., 2019). Peer victimization is often categorized as either relational (e.g., rumors that damage social reputations) or overt (e.g., physical harm), with both forms carrying negative and long-lasting consequences (Cao et al., 2023; Card et al., 2008). Being excluded and victimized by peers threatens a fundamental human need to belong (Baumeister & Leary, 1995), and these experiences are particularly stressful for adolescents (Schriber & Guyer, 2016). Victimization has been linked to earlier onset of substance use (Jiang et al., 2016; Tharp-Taylor et al., 2009). Generally, more substance use is linked with more experiences of peer victimization (Carbone-Lopez et al., 2010; Cénat et al., 2018; Fisher et al., 2016; Hertz et al., 2015; Hong et al., 2022; King et al., 2014; Livingston et al., 2019; McCuddy & Esbensen, 2017; Tretyak et al., 2022; Vieno et al., 2011). For example, Hertz et al. (2015) revealed that being a victim of bullying was associated with greater use of alcohol, cigarettes, and illicit drugs in high school students. In

college students, peer victimization has consistently been associated with substance use (Darabos et al., 2023; Rospenda et al., 2013). Other literature, however, has identified different patterns.

Some studies report no significant association between victimization and substance use (Kaltiala-Heino et al., 2000; Maniglio, 2017; Nansel et al., 2003), including among African-American adolescents (Hong et al., 2018) and among young adults when assessing symptoms of alcohol use disorder (AUD) (Copeland et al., 2013; Takizawa et al., 2014). Additionally, Vannucci et al. (2021) reported a negative association between relational peer victimization and use of marijuana and inhalants among boys, and suggested that relational victimization may exclude boys from social situations in which substances are used in groups. Discrepancies might arise from the timing and duration of victimization exposure, severity, type (verbal, direct, indirect), and the way in which substance use is operationalized (Tretyak et al., 2022). When presenting a conceptual framework about bullying and substance misuse, Hong et al. (2014) suggested that bullying predicts substance misuse with potential mediators and moderators from social experiences, such as perceived support. Adolescents (especially younger adolescents) often turn to parents or other family members for support after being victimized (Hansen et al., 2012), which can reduce effects on substance use (Wormington et al., 2013; Wright, 2016).

Latinx adolescents are more likely to be victimized by peers than their White classmates (Hong et al., 2014; Martin et al., 2018; Vitoroulis & Georgiades, 2017; Vitoroulis & Vaillancourt, 2015), and this risk is compounded by immigration status. Yang and Golshirazi (2023) found that immigrant boys had the strongest association between peer victimization and substance use, compared to girls and U.S.-born adolescents. Social and emotional learning competencies, a construct related to peer competence, attenuated the link between victimization and substance use. Discrimination based on race and/or ethnicity has been associated with higher

substance use (Baiden et al., 2023; Cave et al., 2020; Fuller-Rowell et al., 2012; Pachter et al., 2018; Sapouna et al., 2023). According to Baiden et al. (2023), even occasional discrimination in school predicted 1.52 times higher odds of polysubstance use (i.e., two or more substances) in a predominantly Hispanic (48.9%) and non-Hispanic Black (28.5%) sample. Peer relationships remain crucial during young adulthood, but another context of support and stress particularly salient for young adults is romantic relationships, and the associated risks of romantic rejection.

Romantic Relationships and Substance Use

Social support and romantic rejection as related to substance use have been less studied, and associations with neurobiology even less so. Relationships are developmentally significant during adolescence and a defining feature of the transition to adulthood (Angulski et al., 2018; Collins, 2003; Fleming et al., 2010; Furman et al., 2009; Larson & Sweeten, 2012). Over half of adolescents report being in a romantic relationship, and this number rises to 70% by the age of 18 (Angulski et al., 2018). Positive relationships are a source of social support, whereas negative relationships and dissolution can be overwhelming for adolescents and young adults (Corbin et al., 2020; Fleming et al., 2010). Indeed, rejection and breakups can lead to heightened substance use. Among predominantly Hispanic and Black college students, Larson and Sweeten (2012) found that those who experienced a breakup used significantly more substances. Relationships are key in understanding the interplays of substance use, social stress, and social support.

Prosocial Behaviors and Substance Use

Prosocial behaviors (i.e. engaging in acts such as volunteering) and tendencies (i.e. characteristics such as empathy) are positively associated with indicators of social competence in both adolescence and adulthood (Carlo et al., 2012; Knight et al., 2016; Padilla-Walker et al., 2015), and negatively associated with substance use (Carlo et al., 2011; Carlo et al., 2014; Chen

et al., 2019; Davis et al., 2017; Esparza-Reig et al., 2022; Hassan et al., 2020). Engaging in prosocial behaviors during adolescence has been found to predict lower substance use during young adulthood (Carlo et al., 2011), and early use of substances has been associated with less prosocial behaviors in young women (Davis et al., 2017). Engaging in prosocial behavior was associated with reduced use of cannabis and cigarettes in German adolescents (Frobel et al., 2022). A systematic review on the association between adults' prosocial behavior and addiction problems suggested a negative association, such that adults who reported more prosocial behaviors also reported lower substance use (Esparza-Reig et al., 2022). Symptoms of AUD (e.g., binge drinking) have also been linked to lower prosociality (Tomei et al., 2021). Regarding peers, adolescents who have a high proportion of prosocial friends are less likely to engage in substance use (Barry & Wentzel, 2006; Coyle et al., 2016; Han & Margolin, 2015). In young adults, peer involvement in positive activities is negatively associated with alcohol use (Beard & Wolff, 2020; Stone et al., 2012; Studer et al., 2014). Given that there is evidence of bidirectional associations between substance use and prosociality, the current study examined prosocial characteristics in young adulthood as an indicator of social functioning that could be negatively impacted by substance use in early adolescence.

Neural Response to Social Stimuli

Neural activity during social experiences has not been examined as a mediator between early social experiences and later substance use, or early use and later social functioning, to my knowledge. Some neuroscience literature suggests that social support is rewarding (Bhanji & Delgado, 2014; Fareri & Delgado, 2014; Sazhin et al., 2020), exclusion is distressing (Bolling et al., 2011; Gonzalez et al., 2014; Jenkins & Obhi, 2020; Morese et al., 2019), and substance use is associated with neural response to social stressors (Bach et al., 2019; Gilman et al., 2016a;

Hanlon et al., 2018). Brain regions relevant for the intersection of substance use and social factors include the amygdala, temporoparietal junction (TPJ), anterior insula (AI), sgACC, dACC, ventral striatum (VS), ventromedial (vmPFC) and dorsolateral (dlPFC) regions of the prefrontal cortex, and the periacqueductal gray (PAG) (Bhanji & Delgado, 2014; Blakemore & Mills, 2014; Courtney et al., 2019; Cousijn et al., 2017; Gilman, 2017; Hamidullah et al., 2020).

In adults, social support activates reward-related neural circuitry, including the VS and vmPFC (Fareri et al., 2012; Fareri & Delgado, 2014). Additionally, Fogelman et al. (2021) revealed that adults with higher social support demonstrated less neural activity while viewing alcohol cues in the VS, DS, vmPFC, and PAG. Asscheman et al. (2020) found that more attachment to peers was associated with more insular activity while processing risk information, suggesting higher evaluation and caution, among adolescent boys; thus, a beneficial effect of peer attachment. Additionally, Telzer et al. (2015) revealed a buffering effect of peer support between peer conflict and risk-related neural activity in the striatum and insula. Another study reported that adolescents with higher endorsement of familism had lower VS response to monetary reward during risk-taking, and higher dlPFC response indicating more cognitive control (Telzer et al., 2013). Substance use, however, remains less understood within the context of neural response to social stress.

Using a social influence task, Gilman et al. (2016c) found no behavioral differences in conformity between young adults who used cannabis and those who did not, but they found significant neural differences. Cannabis users showed more NAcc activation while conforming, and this response was positively associated with cannabis use. Another study with the same task found that more caudate response during social influence was linked to more self-reported susceptibility to peers, and that cannabis users had more IFG activity while non-users had more

dlPFC activity (Gilman et al., 2016b). Another study also revealed that adults with AUD demonstrated more neural activity during a socially-stressful task in the right insula, left vPFC, and left middle frontal gyrus (Maurage et al., 2012). In adolescents, a history of being victimized by peers has been linked to more neural sensitivity to social exclusion (Will et al., 2016), neural activity during risky decisions (Rudolph et al., 2016), and neural response to photographs of in-group peers (compared to out-group) during a social judgment task (Telzer et al., 2019). When assessing decisions to donate money, conformity to prosocial peers' donations was positively associated with activity in regions supporting social cognition, salience detection, and reward (Duell & Steinberg, 2020). Regarding romantic rejection, an investigation of adults revealed that viewing photographs of a former romantic partner after a breakup elicited activity in the NAcc and VS, putamen, VTA, OFC, and right lPFC (Fisher et al., 2010).

The literature on social support and neural processing of social stressors is mixed. Some studies found that higher social support was associated with lower activity while experiencing exclusion in Cyberball in the sgACC, dACC, AI, and general PFC (Coan et al., 2006; Eisenberger et al., 2007; Morese et al., 2019; Onoda et al., 2009) including in adolescents (Masten et al., 2012). Other studies, however, found no association (Hyde et al., 2011; Inagaki et al., 2016). Experiences of ethnic-racial discrimination, however, have been associated with neural response to social exclusion via Cyberball. In a study involving Black adults, believing that exclusion was based on race led to greater activation of the rostral ACC (Masten et al., 2011). Further, feeling more distress was related with more activity in the dACC and insula, and less activity in the PFC. With data from the California Families Project (CFP), Schriber et al. (2018) reported that adolescents who experienced a hostile school environment (i.e., violence at school and ethnic-racial discrimination) showed heightened response to exclusion in the sgACC.

Neural response to social exclusion has been associated with risky behaviors in adolescents, and with substance use in adults. After an instance of Cyberball, adolescents in one study demonstrated more activation in the TPJ when making risky decisions, and this activation in turn predicted self-reported risk-taking; however, the link was mediated by RPI (Peake et al., 2013). Falk et al. (2014) showed that neural activity in the dmPFC and TPJ during exclusion predicted increased risky driving behavior when in the presence of a peer in a driving simulation. Further, adolescents with greater activity in regions implicated in rejection (AI, sgACC, and dACC) drove in a riskier manner when accompanied by a same-age passenger, even when controlling for solo driving behavior. Considering that substance use is often a highly social activity, it may be that experiences of rejection motivate adolescents to take risks to regain social status, such as binge drinking at a party to impress peers.

Sensitivity to social exclusion has been assessed in college students who regularly use cannabis, compared to abstainers, revealing that cannabis users displayed atypical neural processing of social exclusion (Gilman et al., 2016a). Young adults who never used cannabis had significant activation in the insula, whereas cannabis users did not. Both groups showed greater vACC activation, but there was an association between vACC activation and self-reported peer conformity only in cannabis users and not in abstainers. The authors suggest that reduced neural sensitivity in the insula might indicate that cannabis users are less aware of social norms. Other work has suggested that adult cocaine users demonstrate greater response to exclusion in the ACC, mPFC, right caudate, and left ventral lateral frontal gyrus (Hanlon et al., 2018). Substance use also influences social brain regions, further contributing to social problems in adults (Jarcho et al., 2022; Sahani et al., 2022; Sazhin et al., 2020). To my knowledge, however, no studies have clarified if neural sensitivity to social exclusion (a uniquely-social stressful event) is related

to substance use in adolescents, as a precursor and/or a consequence; and if neural response mediates associations between social functioning and substance use.

The Current Study

In the existing literature, it is unclear if susceptibility to social stress at the level of the brain contributes is a predictor of substance use in adolescence, an outcome of using substances by early adulthood, or a combination of both. Accordingly, the current study investigated whether neural response to social exclusion (i.e., the brain's activity during a salient social stressor) in mid-adolescence is an explanatory factor between self-reported social support and social stress from late childhood to early adolescence, and later substance use in young adulthood. This study also examined whether neural response was a mediator between early substance use and later social functioning in young adulthood.

One set of hypotheses focused on how early social experiences influenced later substance use, which included that (1) more social support (familism and social support) in late childhood and early adolescence (ages 10 to 14) would predict less substance use in young adulthood (ages 18 to 21), (2) more social stress (peer victimization and racial/ethnic discrimination) would predict more substance use, (3) neural activity during social exclusion and would mediate the paths between early social support and later substance use, (4) neural activity would mediate the paths between early social stress and later use, (5) RPI would also mediate links between social support and substance use, and (6) RPI would mediate links between early social stress and later substance use. Another set of hypotheses centered on how early substance use influences later social functioning, which included that (7) earlier substance use (higher number of years by age 16) would predict worse social functioning in young adulthood, including less social support, lower romantic relationship quality, and less prosocial behaviors, (8) neural activity during social

exclusion and would mediate the relations among early substance use and later social functioning, and lastly, (9) RPI would mediate the relations among early substance use and later social functioning. These associations were tested in a sample of Mexican-origin individuals in a longitudinal study from ages 10 to 23.

Method

Participants

Participants included 229 Mexican-origin adolescents enrolled in a neurobiology substudy of the California Families Project (CFP), an ongoing longitudinal study of children and families. As described previously (Beard et al., 2022a; Johnson et al., 2021; Schriber et al., 2018; Swartz et al., 2020; Weissman et al., 2019), participants in the main CFP study included 674 Mexican-origin families with a fifth-grade child at the time (M_{Age} = 10.4 years, *SD* = 0.61, 50% girls) drawn at random from rosters of schools in Sacramento and Woodland, California. The depression substudy was designed to examine neurobiological mechanisms in the development of depression risk in adolescents.

The depression substudy initially included 229 adolescents (M_{Age} at scan = 17.16 years, *SD* = 0.44, range = 16.24-17.98 years, 49.3% girls), oversampling those with elevated (but sub-clinical) levels of depressive symptoms. Depressive symptoms were measured via counts of adolescents' self-reported symptoms in 9th grade (age 14-15 years) based on the computerized Diagnostic Interview Schedule for Children-IV (DISC-IV) (Shaffer et al., 2000) and the General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (MASQ) (Watson et al., 1995). Adolescents were recruited into the depression substudy if their symptom scores ranged above the median on all three measures of depression (*N* = 43), two measures (*N* = 64), or one measure (*N* = 68); and at or below the median on all three measures (*N*

= 54), to achieve variability. No participants met diagnostic criteria for Major Depressive Disorder at the time. Of the 229 adolescents, 10 were excluded from the MRI scan due to contraindications (e.g., braces) and another 2 were excluded due to equipment malfunction (e.g, task computer shutdown), yielding 217 adolescents who completed all or part of the MRI scan. Another 21 participants were excluded from analyses for reasons of data quality, such as head motion exceeding 1 mm from the previous TR on more than 20% of TRs total. Thus, the final sample analyzed in the present study included 196 individuals who were 51.53% women (see Table 3.1 for sample demographics).

Table 3.1

Sample Demographics

Variable	*N*	*M (SD)*
Gender	Women = 101	
	Men = 95	
Generational Status	1st Gen = 45	
	2nd Gen = 133	
	3rd Gen = 18	
Household Annual Income	< $25,000 = 79	
	$25 - 40 = 58	
	$40 - 55 = 24	
	$55 - 80 = 19	
	> $70,000 = 11	
	Missing = 4	
Household Size		5.38 (1.72)
Maternal Education in Years		9.53 (3.48)

Note: $N = 196$. 1st Gen = Child born in Mexico, 2nd Gen = Child born in U.S. and one parent born in Mexico, and 3rd Gen = Child and both parents born in U.S. Gender and Generational Status were reported at wave 1/age 10, while Household Annual Income, Household Size, and Maternal Education were reported at wave 5/age 14. All participants reported the same gender for each wave.

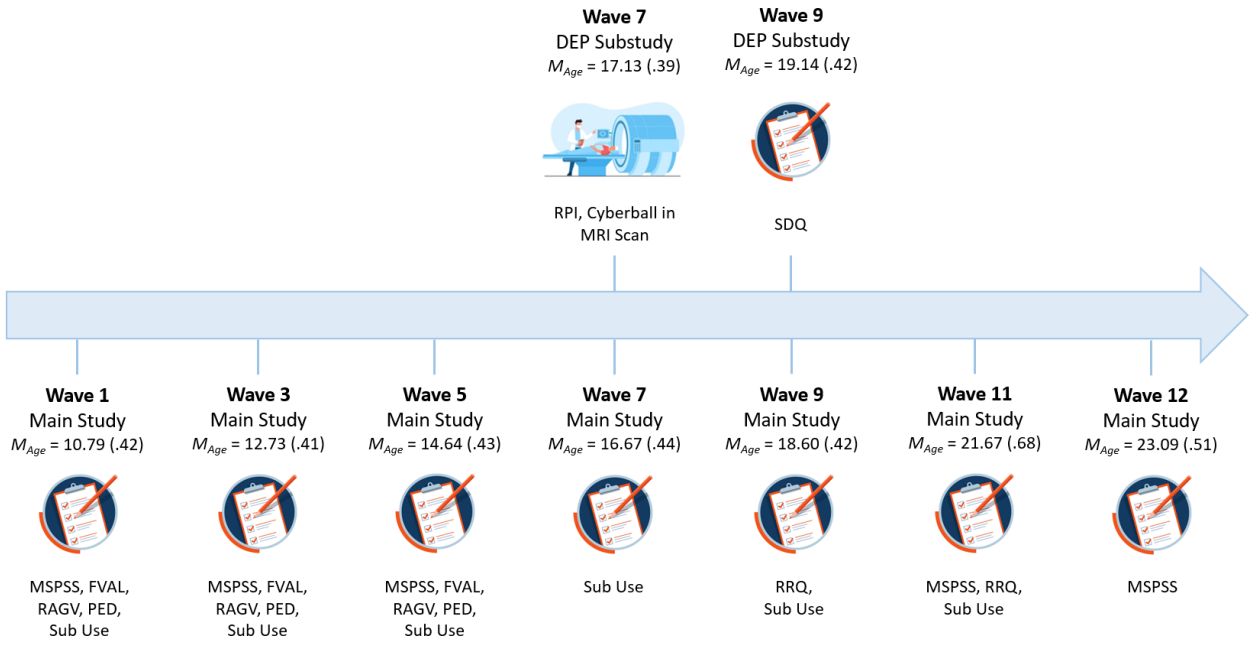
Procedures

All parents gave written informed consent. Adolescents gave assent, and then consent from wave 9 and onwards when they were 18 years old. On the day of the MRI scan, adolescents and one parent visited a research facility in Sacramento, California, where the adolescent participated in an MRI scan composed of a structural scan and three tasks. Participants were asked to abstain from using any substances 48 hours prior to their MRI scan visits. To check for scanning contraindications, participants completed a metal screening form, and those who indicated that they might be pregnant took a pregnancy test. Participants were then instructed about and trained on the Cyberball task (see Measures), and completed a practice session in a

mock MRI scanner to acclimate to the scanning environment. Once inside the scanner, adolescents were given extensive instructions to remain still to decrease head motion, which was also limited with foam padding around the head and surgical tape markers on the face. Outside of the scanner, adolescents completed the Resistance to Peer Influence (RPI) scale and the Strengths and Difficulties Questionnaire (SDQ) (see Measures). All other study variables were assessed independently of the MRI visit, taking place within a range of a few months before the scan or after the scan (see Figure 3.1 for a timeline). The study was approved by the UC Davis institutional review board. Families were compensated with $160 for their participation.

Figure 3.1

Timeline of Data Collection



Note: Values in parentheses reflect standard deviation. MAge = Mean age, DEP = Depression substudy of the California Families Project, MSPSS = Multidimensional Scale of Perceived Social Support (Social Support), FVAL = Family Values subscale of the Mexican-American Acculturation/Enculturation Scale (Familism), RAGV = Relational Aggression Scale: Victim subscale (Peer Victimization), PED = Perceptions and Experiences of Discrimination (Ethnic-Racial Discrimination), RPI = Resistance to Peer Influence, SDQ = Strengths and Difficulties Questionnaire: Prosocial subscale (Prosocial Behaviors), RRQ = Romantic Relationship Quality, and Sub Use = Substance use including items for cigarettes, cannabis, beer, wine, liquor, and

binge drinking occasions during the past three months. N = 196 except for Prosocial Behaviors (n = 175), Social Support Wave 9 (n = 184) and Wave 11 (n = 173), and Relationship Quality Wave 9 (n = 85) and Wave 11 (n = 94). Analyses included Social Support from waves 11 and 12 (instead of 9 and 11) due to a significant change in the questionnaire.

Measures

Substance Use

Substance use was measured via the Alcohol, Tobacco, and Other Drugs (ATOD) survey (Elliott et al., 2006). Participants were asked about their use of six different substances in the past three months: cigarettes, cannabis, beer, wine or wine coolers, hard liquor, and occasions of 5 or more drinks in a row within a few hours (binge drinking) (see Appendix A1 for the survey given to participants). For example, one question asked, "Have you ever tried marijuana, also called a jay, or pot, weed, grass, hash, bud?" If the participant answered *yes*, the follow-up question was, "In the past 3 months, how many times have you used marijuana?" Questions on alcohol use specified "more than just a few sips." The proportion of individuals who had tried at least one substance on at least one occasion from waves 1 to 12 in the current study, had rates similar to those of previous analyses of the main CFP study data from waves 1 to 7 (Atherton et al., 2016; Clark et al., 2020; Cruz et al., 2019). Response options included: 1 (*Never*), 2 (*Less than Once per Week*), 3 (*About Once per Week*), 4 (*Two to Three Times per Week*), and 5 (*Almost Every Day*). Refusal to answer was coded as 8 and "Don't know" was coded as 9, both treated as missing. Responses were recoded to range from 0 (*Never*) to 4 (*Almost Every Day*). Answering "no" to a question about ever trying a substance resulted in a score of 0 for past 3 months' use. Higher scores represent greater use of substances.

Responses about past 3 months' use at wave 9/age 18, wave 11/age 21, and wave 12/age 23 were summed into a composite score, for analyses involving early social functioning in late childhood to early adolescence and later substance use in young adulthood. The maximum score

possible was 48 (6 substances X 4 response for daily/almost daily use X 2 waves). To control for previous history of use, a dichotomous variable was also calculated for lifetime use by wave 5/age 14 and entered as a covariate into analyses of early social functioning and later substance use. Values were 0 if a participant never tried any substance in their lifetime, or 1 if a participant had tried at least type of substance on at least one occasion. For analyses involving early substance use and later social functioning, another variable was created to assess how long adolescents had been using substances by wave 7/age 16. Years of substance use was calculated by subtracting a participant's age of first use of any substance (cigarettes, cannabis, beer, wine, and liquor) from their current age at wave 7. A previous CFP project using a similar approach with data from a separate substudy (Weissman et al., 2015) reported that years of substance use ranged from 0 = never reported having used substances and none detected at MRI visit, to 7 = reported having used substances for the first time at age 10, with 28% of adolescents reporting 0 years, 36% between 1 and 3 years, 32% between 4 and 6 years, and 4% reporting 7 years. Higher scores indicate earlier substance use.

Table 3.2

Reliability of Measures across Waves

	Wave 1	Wave 3	Wave 5	Wave 7	Wave 9	Wave 11	Wave 12
Variable	*α*	*α*	*α*	*α*	*α*	*α*	*α*
Substance Use					.76	.78	.80
Substance Use Sum W9-11						.74	
Years of Substance Use				.86			
Social Support	.85	.90	.90			.96	.93
Familism	.73	.73	.78				
Peer Victimization	.90	.81	.81				
Ethnic-Racial Discrimination	.74	.74	.92				
Relationship Quality					.88	.92	
Resistance to Peer Influence				.76			
Prosocial Behaviors					.74		
Post-Cyberball Task Experience				.74			
Post-Cyberball Need Threat				.91			

Note: N = 196. α = Cronbach's alpha, W9 = Wave 9/age 18, W11 = Wave 11/age 21, and W12 = Wave 12/age 23. Analyses included Social Support from waves 11 and 12 (instead of 9 and 11) due to a significant change in the questionnaire.

Social Support

Social Support was assessed every other year with the Multidimensional Scale of Perceived Social Support (MSPSS) (Zimet et al., 1988). Two subscales with 4 items each were given to capture how much support participants perceived from their friends and family, such as "You can talk about your problems with your [friends/family] when things go wrong." Response options ranged from 1 (*Not at All True*) to 4 (*Very True*). These two subscales were administered from wave 1/age 10 to wave 5/age 14 resulting in 8 items for each wave. During wave 11/age 21, the measure changed to combine the two categories into one such that 4 items were administered; for example, "Your family and friends are willing to help you make decisions." Thus, the current study relied upon data from wave 11/age 21 and wave 12/age 23, rather than waves 9 and 11 similar to other study variables assessing social functioning in young adulthood

(see Figure 3.1). Mean scores were computed for waves 1, 3, and 5; and then for waves 11 and 12. Higher scores represent more perceived support from family and friends.

Familism

Familism was assessed every other year with a 16-item subscale of the Mexican American Cultural Values Scale (Knight et al., 2010). The subscale includes different aspects of traditional family values, such as family support (responsibility to maintain close relationships to the family including extended family members), family as a referent (importance of how your actions reflect upon the family such as considering them in decisions), and family obligations (expectation to help family such as taking care of siblings). A sample item is, "Family provides a sense of security because they will always be there for you," using responses from 1 (*Not at All True*) to 4 (*Very True*). For the current study, a mean score was computed with 8 items at waves 1, 3, and 5 (Appendix A1). Higher scores represent more endorsement of familism values.

Peer Victimization

During every other year of the CFP, peer victimization was assessed with the 18-item Relational Aggression scale adapted from Prinstein et al. (2001), Neary and Joseph (1994), and Kokkinos and Panayiotou (2004). In this scale, 9 items evaluated to what extent the participant was a perpetrator of physical, verbal, or emotional aggression against others; and 9 items evaluated being a victim of these types of aggression. The Victim subscale was used in the present study, with items such as, "In the past 3 months, a kid your age left you out of what he or she was doing." Each statement was rated on a 4-point scale from 1 (*Almost Never or Never*) to 4 (*Almost Always or Always*). A mean score was computed for peer victimization across waves 1/age 10, 3/age 12, and 5/age 14. Higher scores indicate more experiences of victimization.

Ethnic-Racial Discrimination

Experiences of discrimination based on race/ethnicity was measured every other year with the Perceptions of Discrimination and Personal Experiences with Discrimination (PDPED) questionnaire, a measure of discrimination against Mexicans/Mexican-Americans youth that they experienced at school (Johnston & Delgado, 2004). This scale was created based on the Racism in the Workplace Scale (Hughes & Dodge, 1997) and the Schedule of Sexist Events (Klonoff & Landrine, 1995). Ethnic-racial discrimination by one's peers was assessed with five items drawn from the DSCR, capturing participants' experiences of peers as a source of discrimination based on their ethnic-racial background, such as the item, "Kids at school think bad things about Mexicans/Mexican-Americans." Responses were on a 4-point Likert scale ranging from 1 (*Not at All True*) to 4 (*Very True*). For the current study, a mean score was computed with waves 1, 3, and 5. Higher scores indicate greater experiences of ethnic-racial discrimination.

Romantic Relationship Quality

Romantic relationship quality at wave 9/age 18 and wave 11/age 21 was assessed with a novel scale in the CFP developed from diverse sources, including a measure of marital quality (Norton, 1983) and marital instability (Yeh et al., 1983). Six items were rated on a 4-point Likert scale ranging from 1 (*Not at All True*) to 4 (*Very True*). A sample item is, "My relationship with my partner makes me happy." A low score on quality can be interpreted as a social stressor relevant for young adults in this study. A mean score was computed with waves 9 and 11, with higher scores indicating a higher-quality relationship. Participants rated the quality only if they reported currently being in a relationship at the time of the study visit (n = 85 at wave 9/age 18; and n = 94 at wave 11/age 21).

Resistance to Peer Influence

The Resistance to Peer Influence (RPI) Scale (Steinberg & Monahan, 2007) was administered during the depression substudy at wave 7/age 16 to measure adolescents' perceptions of their tendency to conform to, or resist conforming to, the attitudes and behaviors of their peers. The RPI consists of 10 different scenarios with conflicting statements regarding peer influence (e.g., "Some friends go along with their friends just to keep their friends happy, BUT Other people refuse to go along with what their friends want to do, even though they know it will make their friends happy"). In this study, participants rated how true each statement was on a scale of 1 to 4, with a lower score reflecting a preference for statement 1 while a higher score reflects a preference for statement 2. For example, participants would indicate 1 (*Really True of Me*) if the first statement is much more applicable, 2 (*Sort of True of Me*) if the first statement is somewhat applicable, 3 (*Sort of True of Me*) if the second statement is somewhat applicable, or 4 (*Really True of Me*) if the second statement is much more applicable. Higher average scores indicate greater resistance to peer influence (i.e., less social conformity), whereas lower scores indicate less resistance to peer influence (i.e., greater social conformity).

Prosocial Behaviors

The current study relied upon the Strengths and Difficulties Questionnaire (SDQ), a 25-item measure capturing social, emotional, and behavioral strengths and difficulties (Goodman, 1997), collected at wave 9/age 19. The 5-item Prosocial Behaviors subscale asked participants to rate themselves on how true certain statements were of them, such as "Helpful if someone is hurt, upset or feeling ill," with response options from 1 (*Not True*) to 3 (*Certainly True*). Higher scores indicate more engagement in general prosocial behaviors.

Post-Cyberball Task Experience

Approximately 20 minutes after Cyberball, adolescents were asked to rate how much they felt included and excluded during the game, with response options from 1 (*Not at All*) to 5 (*Very Much So*). Questions also assessed emotional distress, such as "I feel…" 1 (*Relaxed*) to 7 (*Tense*), as well as what percentage of the time the ball was thrown to them as a manipulation check. Higher scores represent more feelings of exclusion and distress. A mean score was computed to evaluate how socially excluded participants felt after the task.

Post-Cyberball Need Threat

In addition to task experience, subjective distress was measured with the Need-Threat Scale (Masten et al., 2009; Williams et al., 2000). This 12-item questionnaire asked adolescents about experienced consequences that threaten 4 basic human needs: self-esteem, belongingness, meaningfulness, and sense of control. For example, a sample item for self-esteem is, "I felt good about myself," rated on a scale of 1 (*Not at All*) to 5 (*Very Much*). The current study relied upon a mean score to evaluate to what extent adolescents felt distress due to their needs being threatened during the task.

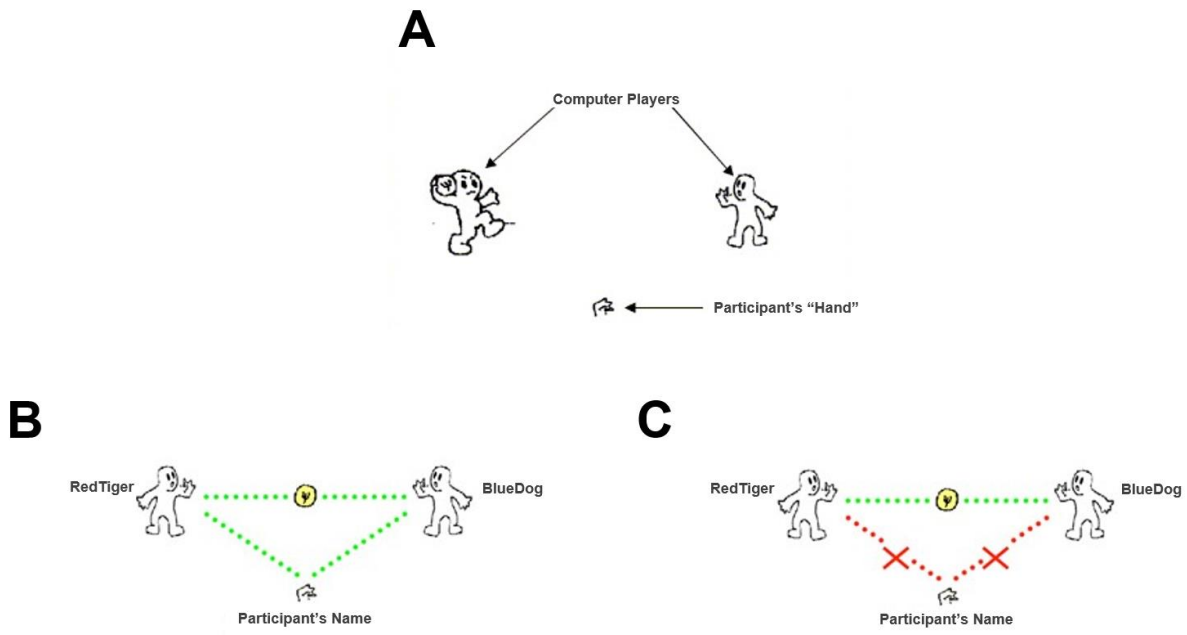
Cyberball Task Design

The Cyberball task (Eisenberger & Lieberman, 2003) was completed during an MRI scan to measure neural response to social inclusion, as a form of social reward. Figure 3.2 shows examples of inclusion trials and exclusion trials, similar to the adapted Cyberball task design used in the current study, as described in past CFP work (Beard et al., 2022a; Schriber et al., 2018). Participants were told they would play a virtual ball-tossing game with two computerized players and asked to imagine, as vividly as possible, that they were playing with other individuals of the same age. On the screen, participants saw cartoon figures and usernames representing two other players (of no apparent gender or race/ethnicity), their own cartoon

"hand" controlled via a button box, and a username chosen during this session. During the game, the ball was thrown back and forth among all three players. Participants chose the recipient of their throws using the button box, whereas throws of the two other players were selected by the computer program.

Figure 3.2

Cyberball Task Design



Note: The Cyberball task presents the participant with two computer players and a representation of their own cartoon hand (A). Inclusion trials (B) involve the participant receiving ball tosses from the other two players, whereas Exclusion trials (C) involve the two other players passing the ball to each other and leaving out the participant. Avatar names were randomly generated and included no information about gender, race, ethnicity, or other identifying features.

While in the MRI scanner, participants played 12 rounds of Cyberball, with six rounds of Inclusion and six rounds of Exclusion, always presented in the same pseudorandom order: Inclusion, Exclusion, Inclusion, Inclusion, Exclusion, Inclusion, Exclusion, Inclusion, Exclusion, Exclusion, Exclusion, and Inclusion (Schriber et al., 2018). In Inclusion rounds, the other players were equally likely to throw the ball to the participant or each other. However, during Exclusion

rounds, the other players stopped throwing the ball to the participant and continued throwing it only to each other. Each round lasted 36 sec, being comprised of a fixation point (4 sec), "Begin Match!" notification (2 sec), and 10–11 ball tosses of game play (22–23 sec) that included all relevant players' ball tosses, followed by a short reloading screen (7–8 sec). There were also Instructions (8 sec) at the start and a "Thank you!" (3 sec) at the end signifying completion of the task. The functional scan lasted 7 min and 23 sec implemented in one run.

Cyberball fMRI Acquisition & Analysis

Participants underwent scanning on a research-dedicated 3T Siemens Tim Trio whole-body MRI system (Siemens Medical Solutions, Erlangen, Germany) with a 32-channel head coil. Following sagittal localization and a manual shim procedure, whole-brain BOLD functional T2*-weighted echo-planar images (EPI) were acquired for each volume. Following EPI collection, a high-resolution structural scan was acquired using a T1-weighted standardized magnetization-prepared spoiled gradient recalled echo pulse sequence for spatial normalization with 208.95-mm slices, a repetition time (TR) of 2500 ms, a time-to-echo (TE) of 4.33 ms, a field-of-view (FOV) of 243 mm with a 7-degree flip angle, an inversion time of 800 ms, and a 256 x 256 mm matrix. During the Cyberball task, functional scans consisted of 126 contiguous T2*- weighted echo planar imaging whole-brain volumes, including 35 interleaved 3.5 mm thick slices per brain volume, oriented to the anterior commissure and posterior commissure line and encompassing the entire cerebrum and the majority of the cerebellum. Scan parameters were as follows: 64 x 64 matrix; TR = 2000 ms; TE = 27 ms; flip angle = 80°; FOV = 224 mm; and voxel size = 3.5 x 3.5 x 3.5 mm. The first two volumes were discarded to allow for equilibration of saturation effects.

All preprocessing and analyses were conducted in Analysis of Functional NeuroImages (AFNI: www.afni.nimh.nih.gov/afni, version 16.2.09; Cox, 1996). Preprocessing of functional

EPI data consisted of several stages: interleaved slice-timing correction, image realignment to the third volume, rigid body motion correction using all 6 parameters, and co-registration of functional data with extracted structural images normalized to Montreal Neurological Institute (MNI) stereotaxic space. Alignment was visually confirmed for participants. Subsequently, spatial smoothing with a 6-mm, full-width at half-maximum Gaussian kernel was conducted to increase the signal-to-noise ratio and adjust for individual variability in anatomy. Volumes with head motion >1 mm from the previous volume were censored during further processing.

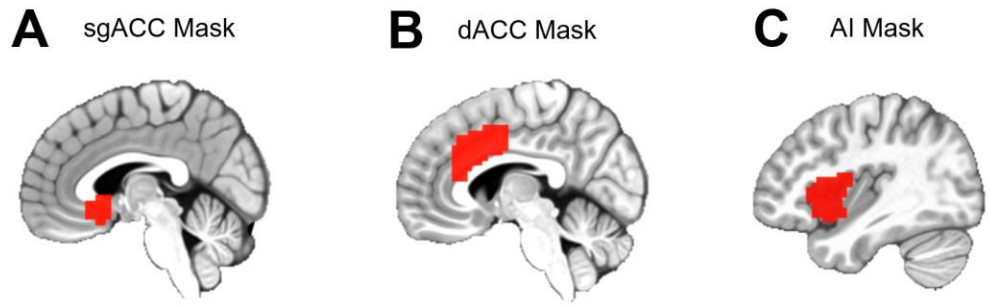
For first-level analyses, Cyberball was modeled as a block design consisting of Inclusion or Exclusion conditions. The time series of 126 image volumes was deconstructed into five regressors, each included in the design matrix. These consisted of Inclusion, Exclusion, instruction screen, “Begin match!” screen, and button presses (mostly during Inclusion) to control for motor activity. The last three were regressors of no interest. Exclusion and Inclusion were modeled as boxcar functions with an amplitude of 1 using AFNI’s duration modulation (dmBLOCK) to account for duration variability due to reaction time differences. Other regressors of interest were modeled using gamma functions. All were convolved with a canonical hemodynamic response function. The six motion parameters were modeled as effects of no interest to account for variance due to head movement. Finally, time periods showing the beginning fixation point, end reloading, and final “Thank you!” screens were not modeled to maintain an implicit baseline. Linear contrasts were calculated that compared blood-oxygen level–dependent (BOLD) responses in the Exclusion > Baseline conditions for each participant.

A structural region-of-interest (ROI) approach was used to assess BOLD responses to Exclusion > resting baseline, within the sgACC, dACC, and AI. The ROIs for right and left sgACC were created from right and left Brodmann Area (BA) 25 masks as defined by the

Talairach-Tournoux database within AFNI, transformed to MNI space using the tta2mni function, then modified to include only areas of BA 25 that were under the genu of the corpus callosum posterior to y = 30 and identifiable (including through using AFNI's whereami function in MNI space) as “cingulate cortex.” Activation within the resulting ROI was similar to significant clusters of activation reported in Cyberball studies on adolescents (e.g., Masten & Eisenberger, 2011). For the dACC, right and left ROIs were created using the “cingulate cortex” mask in the MNI database modified to use a rostral boundary of y = 32, consistent with previously established criteria (Vogt et al., 2003). For the AI, right and left ROIs were created from the “insula” mask in the MNI database modified to use all voxels anterior to the y = 0 plane (Beard et al., 2022a). For all three ROIs, right and left masks were averaged to create bilateral masks, shown in Figure 3.3. Within each ROI mask, per-participant average beta values for the linear contrast of Exclusion > Baseline were extracted for further analysis.

Figure 3.3

Masks Created for Region-of-Interest Analyses of Social Exclusion



Note: sgACC = Subgenual anterior cingulate cortex, dACC = Dorsal anterior cingulate cortex, AI = Anterior insula.

Data Analysis

Statistical analyses were conducted in RStudio version 2023.6.0.421 (RStudio Team, 2023) and SPSS Statistics version 28.0 (IBM Corp, 2021). Variables were checked for outliers

and non-normality, and outliers were winsorized to within 3 *SD* of the mean. Gender and depression recruitment status were included as covariates in all analyses, and previous substance use by wave 5/age 14 was included as a covariate for models involving early social functioning and later substance use. Depression recruitment status represents the risk of depression ("Low" or "Elevated") based on self-reported symptoms in the ninth grade (age 14-15 years) from the computerized DISC-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the MASQ (Watson et al., 1995). Preliminary analyses included zero-order correlations. Main analyses were double-mediation models within a structural equation modeling (SEM) framework, using seven time points of self-reported data and one time point of bilateral sgACC, dACC, and AI responses to social exclusion during the Cyberball task. Model fit was considered excellent if: CFI $\geq$ 0.90, TLI $\geq$ 0.90, RMSEA $\leq$ 0.08, and SRMR $\leq$ 0.08 (Hooper et al., 2008; Hu & Bentler, 1999; Kline, 2023). Mediation models are useful in describing how one variable (e.g., early social stress) has an effect on another variable (e.g., later substance use) through its influence on an intermediate variable (e.g., neural response to social exclusion in the dACC) (Selig & Preacher, 2009). Longitudinal data adds complexity, but also the possibility of making more causal claims, inferences can be made that earlier variables precede later variables. One set of models tested early social stress and support as the predictors, whereas other models tested substance use as the predictor, to better capture if social functioning is a risk factor for substance use later on *or* if early substance use is a risk factor for later social stress.

Results

Preliminary Analyses

Descriptive statistics for all variables are presented in Table 3.3. Results from neuroimaging ROI analyses with the contrast Social Exclusion > Baseline are shown in Figure

3.4, and corresponding *t*-values and peak coordinates are shown in Table 3.4. Social exclusion elicited significant neural activity in the left and right sgACC, dACC, and AI. Left and right hemisphere values were averaged and bilateral activity was used in further analyses. As shown in Table 3.3, average substance use during the past 3 months was very low at wave 1/age 10 and wave 3/age 12, increased but remained low at wave 5/age 14 and wave 7/age 16, increased substantially at wave 9/age 18, and then again at wave 11/age 21 when most participants (85%) were of legal drinking age. By wave 7/age 16, average years of substance use was relatively low; but 53% (N = 104) of adolescents had reported trying at least one type on at least one occasion. Figure 3.5 displays longitudinal changes in the percentage of substance use in participants' lifetime (Figure 3.5A) and during the past 3 months (Figure 3.5B). Lifetime incidence rates from waves 1-11 were similar to those of previous publications involving data from the main CFP study, such as the rates from waves 1-7 (N = 674) reported by Atherton et al. (2016).

Social support was relatively high across waves with little change (Table 3.3), and familism was high in wave 3/age 12 and wave 5/age 14. Peer victimization and ethnic-racial discrimination were relatively low. Resistance to peer influence (RPI) was relatively high at wave 7/age 16. After playing Cyberball in the MRI scanner, adolescents reported feeling included for 32% of throws and excluded for 60% of throws; and they felt significantly more excluded than included (paired t_{187} = 9.01, p < .001). For young adults in romantic relationships, quality ratings were relatively high at wave 9/age 18 (n = 85) and wave 11/age 21 (n = 94).

Bivariate correlations are presented in Table 3.5. Neural response to social exclusion was positively associated among the sgACC, dACC, and AI. Years of substance use by wave 7/age 16 was negatively associated with early social support and familism, whereas the sum of substance use from wave 9/age 18 to wave 12/age 23 was negatively associated with romantic

relationship quality and familism. Social support in early adolescence and young adulthood was positively associated with familism, prosocial behaviors, and romantic relationship quality; and social support during early adolescence in particular was negatively associated with peer victimization and ethnic-racial discrimination. Familism was positively related with romantic relationship quality and RPI, and negatively related with peer victimization and ethnic-racial discrimination. Peer victimization was positively linked to ethnic-racial discrimination, and prosocial behavior was positively linked to relationship quality. RPI was positively associated with prosocial behaviors. Activity in the sgACC during social exclusion was positively associated with lifetime substance use (a covariate included in analyses of early social functioning and later substance use), and greater prosocial behavior was associated with greater activity in the dACC and AI. No other significant correlations emerged among neural activity and other study variables. Girls reported more experiences of ethnic-racial discrimination, and more prosocial behaviors.

Table 3.3

Descriptive Statistics for Study Variables

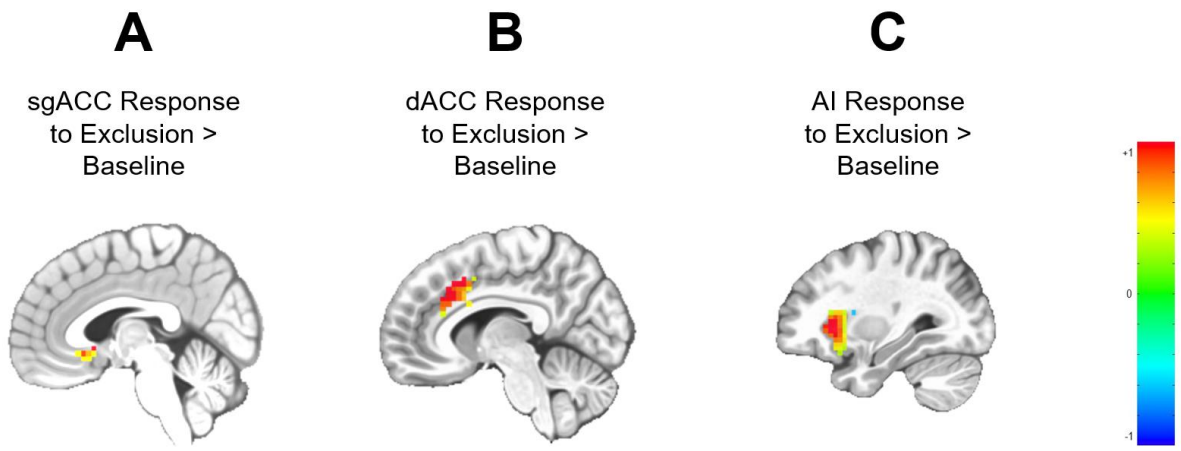
	Wave 1	Wave 3	Wave 5	Wave 7	Wave 9	Wave 11	Wave 12
Variable	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*
Cigarettes	0 (0)	.02 (.15)	.03 (.24)	.05 (.28)	.08 (.44)	.24 (.80)	.30 (.75)
Cannabis	0 (0)	.01 (.10)	.18 (.62)	.34 (.93)	.37 (1.01)	.57 (1.17)	.71 (.94)
Beer	.02 (.22)	.04 (.25)	.14 (.42)	.17 (.48)	.29 (.65)	.98 (.87)	1.38 (.85)
Wine	.01 (.14)	.01 (.10)	.07 (.27)	.09 (.30)	.16 (.42)	.38 (.60)	.50 (.58)
Liquor	0 (0)	0 (.07)	.14 (.44)	.18 (.50)	.30 (.60)	.64 (.87)	.81 (.85)
Binge Drinking	.01 (.07)	.02 (1.5)	.04 (.25)	.02 (.21)	.18 (.48)	.63 (.67)	.79 (.71)
Substance Use (Sum)	.04 (.42)	.11 (.82)	.59 (2.23)	.85 (2.70)	1.39 (3.58)	3.41 (4.99)	4.49 (4.68)
Years of Cigarettes				.55 (1.46)			
Years of Cannabis				1.81 (1.12)			
Years of Beer				2.76 (.89)			
Years of Wine				.75 (1.30)			
Years of Liquor				1.68 (.92)			
Years Substance Use				1.51 (1.14)			
Previous Substance Use			.37 (48)				
Depression Recruitment Status			.80 (.40)				
Social Support	3.08 (.77)	3.19 (.78)	3.18 (.75)		3.13 (.89)	3.37 (.82)	3.36 (.73)
Familism	2.68 (.79)	3.43 (.42)	3.41 (.40)				
Peer Victimization	1.46 (.53)	1.14 (.25)	1.10 (.20)				
Ethnic-Racial Discrimination	1.35 (.34)	1.17 (.21)	1.22 (.25)				
Relationship Quality					3.75 (.39)	3.69 (.48)	
Resistance to Peer Influence				3.09 (.49)			
Prosocial Behaviors (Sum)					7.41 (1.91)		
sgACC Response to Social Exclusion				-.06 (.19)			
dACC Response to Social Exclusion				-.05 (.15)			
AI Response to Social Exclusion				-.03 (.16)			
Post-Cyberball Task Experience				2.81 (.96)			
Post-Cyberball Need Threat				2.97 (.86)			

Note: N = 196 except for Prosocial Behaviors (N = 175), Social Support waves 9 (N = 184) and 11 (N = 173), and Relationship Quality waves 9 (N = 85) and 11 (N = 94). sgACC = Subgenual anterior cingulate cortex, dACC = Dorsal anterior cingulate cortex, AI = Anterior insula. Previous Substance Use is coded as 0 = None, 1 = At least once. On average, Wave 1 represents age 10, Wave 3 represents age 12, Wave 5 represents age 14, Wave 7 represents age 16, Wave 9 represents age 18, Wave 11 represents age 21, and Wave 12 represents age 23. Substance use

was reported as past 3 months. Analyses included Social Support from waves 11 and 12 (instead of 9 and 11) due to a change in the questionnaire. Mean values presented unless otherwise noted.

Figure 3.4

Contrast Maps from Region-of-Interest Analyses of Social Exclusion



Note: N = 196. sgACC = Subgenual anterior cingulate cortex, dACC = Dorsal anterior cingulate cortex, AI = Anterior insula. Bilateral activity is shown for the contrast of Social Exclusion > Baseline with a minimum threshold $t = 2.575$, $p < .05$ corrected for each search region.

Table 3.4

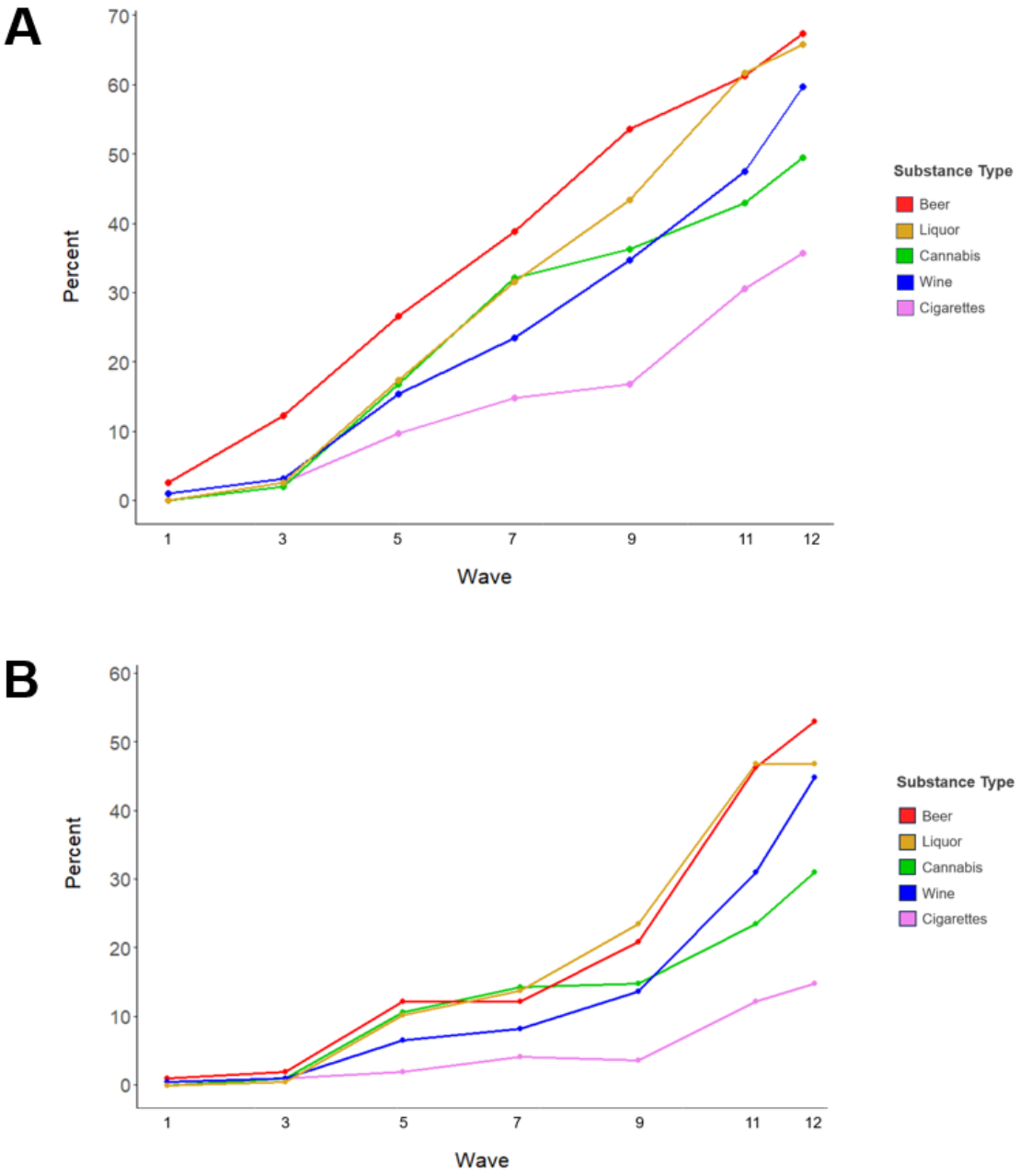
T-statistics and Peak Coordinates from Region-of-Interest Analyses of Social Exclusion

	Statistic	Peak Coordinates (MNI)		
Region	*t*	x	y	z
L sgACC	2.97*	-2	19	-5
R sgACC	2.81*	3	21	-6
L dACC	3.68*	-5	1	42
R dACC	3.52*	4	5	38
L AI	4.97*	-33	22	-1
R AI	4.12*	29	20	-3

Note. *N* = 196. * indicates *p*-corrected < .05. R and L = Right and left hemispheres, respectively. sgACC = Subgenual anterior cingulate cortex, dACC = Dorsal anterior cingulate cortex, and AI = Anterior Insula. x, y, and z = Montreal Neurological Institute coordinates in the left–right, anterior–posterior, and inferior–superior dimensions, respectively. *t* = *t*-score for the contrast of Social Exclusion > Baseline at the given coordinates (local maxima), with a minimum threshold *t* = 2.575, *p* < .05 corrected for each search region.

Figure 3.5

Cumulative Percentage of Participants Reporting Substance Use Over Time



Note: N = 196. On average, Wave 3 represents age 12, Wave 5 represents age 14, Wave 7 represents age 16, Wave 9 represents age 18, Wave 11 represents age 21, and Wave 12 represents age 23. Lifetime use (A) is defined as at least one occasion of trying the substance at any time, whereas Past 3 Months (B) is defined as frequency of use during the past 3 months with responses ranging from 0 (Never) to 5 (Almost Every Day).

Table 3.5

Bivariate Correlations among Study Variables

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1. Gender	1															
2. Depression Recruitment Status	.01	1														
3. Substance Use W9-11	.01	.06	1													
4. Years of Substance Use by W7	.03	.05	.29**	1												
5. Previous Substance Use before W5	-.02	.01	.38**	.78**	1											
6. Social Support W1-5	.01	.03	-.18*	-.29**	-.18**	1										
7. Social Support W11-12	-.11	.07	-.04	-.20**	-.10	.41**	1									
8. Familism W1-5	-.08	.07	-.16*	-.25**	-.15*	.71**	.34**	1								
9. Peer Victimization W1-5	-.10	.01	.02	.01	.03	-.34**	-.09	-.35**	1							
10. Ethnic-Racial Discrimination W1-5	-.21**	.12	.09	.10	.07	-.19**	-.09	-.15†	.52**	1						
11. Relationship Quality W9-11	-.10	.00	-.18*	-.08	-.10	.22**	.21**	.26**	-.08	-.01	1					
12. Resistance to Peer Influence W7	-.09	.07	-.05	-.14†	-.10	.09	.21**	.18*	-.07	-.03	.16†	1				
13. Prosocial Behaviors W9	-.21**	.07	-.07	-.04	-.01	.34**	.17†	.31**	-.10	-.05	.18*	.22*	1			
14. sgACC Response to Social Exclusion W7	.04	.05	.11†	-.08	.15*	-.11	-.07	.01	.02	.05	.05	-.04	-.09	1		
15. dACC Response to Social Exclusion W7	.12	.01	-.02	-.09	-.05	-.07	-.03	-.06	-.01	-.01	-.04	.01	.39**	-.04	1	
16. AI Response to Social Exclusion W7	.11	-.13†	-.09	.06	.05	-.01	-.07	.02	-.05	-.02	-.08	-.04	.23**	.36**	-.01	1
17. Post-Cyberball Need Threat W7	-.21*	.07	-.03	-.06	.02	-.02	-.02	-.06	.04	.09	.12	-.01	.23*	.03	-.05	.15*

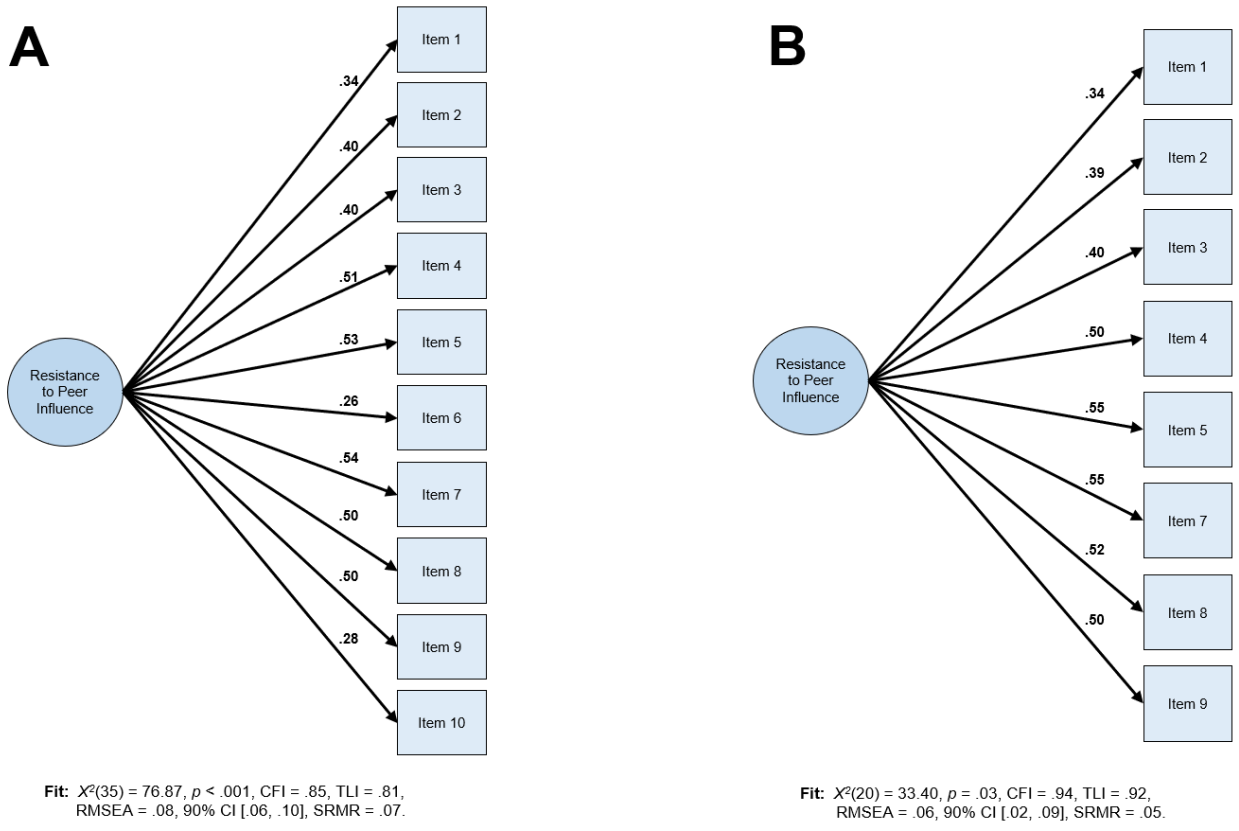
Note: N = 196 except for Social Support W9-11 (*N* = 194), Prosocial Behaviors (*N* = 175), and Relationship Quality (*N* = 85). sgACC = Subgenual anterior cingulate cortex, dACC = Dorsal anterior cingulate cortex, AI = Anterior insula, W1 = Wave 1/age 10, W3 = Wave 3/age 12, W5 = Wave 5/age 14, W7 = Wave 7/age 16, W9 = Wave 9/age 18, W11 = Wave 11/age 21, and W12 = Wave 12/age 23. W1-5 reflects average across Waves 1, 3, and 5. W9-11 reflects average across Waves 9 and 11. Substance Use is the sum of reported use in the past 3 months, Previous Substance Use was reported as yes/no (0/1) at Wave 5, and Years of Substance Use was calculated by subtracting age of first use from current age at Wave 7. Gender is coded as 0 = Women, 1 = Men. Higher scores on Post-Cyberball Need Threat represent greater self-reported distress during the task. Analyses included Social Support from waves 11 and 12 (instead of 9 and 11) due to a significant change in the questionnaire.

Measurement Models

Latent factor structure for RPI at wave 7/age 16 and prosocial behaviors at wave 9/age 18 was tested with confirmatory factor analyses. Regarding RPI, the original model with 10 items showed poor fit and one question with low factor loadings (Figure 3.6A); thus, that item was dropped, resulting in good model fit (Figure 3.6B). The dropped question was, "Some people will not break the law just because their friends say that they would, BUT Other people would break the law if their friends said that they would break it." The 9-item latent factor was entered into further analyses. Prosocial behaviors at wave 9/age 18 had excellent model fit (Figure 3.7).

Figure 3.6

Confirmatory Factor Analyses of Resistance to Peer Influence

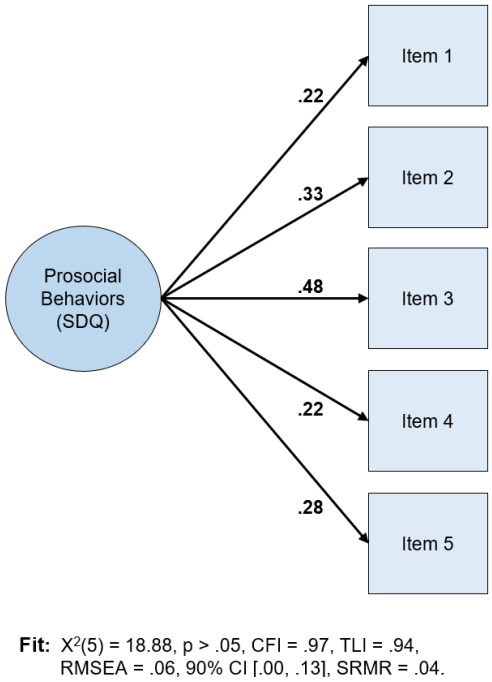


Note: N = 196. X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker

Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, and SRMR = Standardized root mean square residual. Standardized estimates presented. Panel A reflects the original model with 10 items and Panel B reflects the reduced model with 8 items. Data were collected during Wave 7 when participants were approximately age 16.

Figure 3.7

Confirmatory Factor Analysis of Prosocial Behaviors



Note: N = 196. SDQ = Strengths and Difficulties Questionnaire, X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, and SRMR = Standardized root mean square residual. Standardized estimates presented. Data were collected during Wave 7 when participants were approximately age 16.

Next, analyses involving social support and social stress are reported. All analyses reported below include the covariates gender (coded as "*0 = Women*") and depression risk status (coded as "*0 = Low*"); and analyses involving early social functioning and later substance use include previous substance use by wave 5/age 14 as a covariate (coded as "*0 = Never tried any substance*" or "*1 = Tried at least one substance on at least one occasion in lifetime*").

Social Support, Brain Activity during Exclusion, and Substance Use

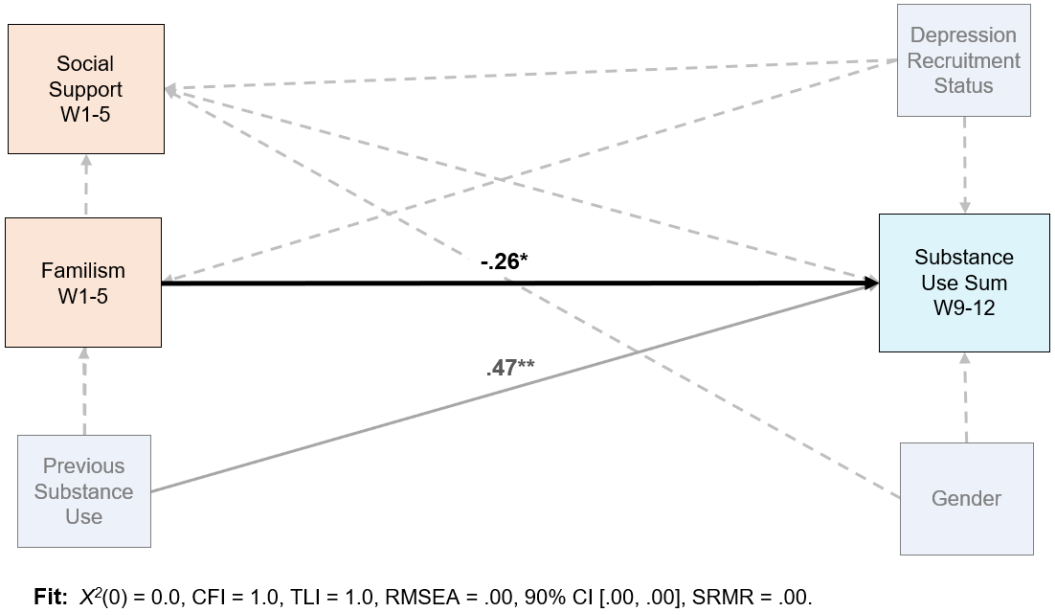
In the path analysis, familism was negatively associated with substance use during young adulthood (sum across wave 9/age 18, wave 11/age 21, and wave 12/age 23), as shown in Figure 3.8. When examining each predictor separately, higher social support predicted lower substance use (Table 3.6). In the SEM with mediators RPI and neural response to social exclusion (in the sgACC, dACC, and AI), sgACC activity was negatively associated with social support and positively associated with substance use (Figure 3.9). The indirect effect, however, was not significant, β = -.44, p = .11. Results of Sobel's test also suggested no full mediation effect as the indirect effect was not significantly different from zero, z = -1.52, SE = .35 p = .12. The direct effect of social support on substance use without sgACC activity or other predictors in the model (i.e., with only covariates in the model) was significant, β = -1.15, p = .008. Thus, there was a partial mediation effect of sgACC activity between early social support and later substance use.

When assessing social support alone, there were no significant associations among social support, RPI, neural activity, or later substance use (Table 3.7). This pattern suggests that controlling for familism is important. When examining familism alone, higher familism was associated with higher RPI (i.e., lower susceptibility to peer influence) and lower substance use. Familism was not significantly associated with neural activity during social exclusion. In sum,

endorsing higher familism led to less substance use during young adulthood, and sgACC response to exclusion partially mediated a link between social support and later substance use.

Figure 3.8

Path Model with Social Support and Familism Predicting Substance Use



Note: $N = 196$. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$. X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, SRMR = Standardized root mean square residual, W1 = Wave 1/age 10, W3 = Wave 3/age 12, W5 = Wave 5/age 14, W7 = Wave 7/age 16, W9 = Wave 9/age 18, W11 = Wave 11/age 21, W12 = Wave 12/age 23, and Depression Recruitment Status = Depression recruitment status, coded as 0 = Low and 1 = Elevated, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (Watson et al., 1995). Gender is coded as 0 = Women, 1 = Men. Social Support and Familism reflect averages across waves 1, 3, and 5. Substance Use Sum reflects an average of waves 9, 11, and 12 with cigarettes, cannabis, beer, wine, liquor, and binge drinking.

Table 3.6

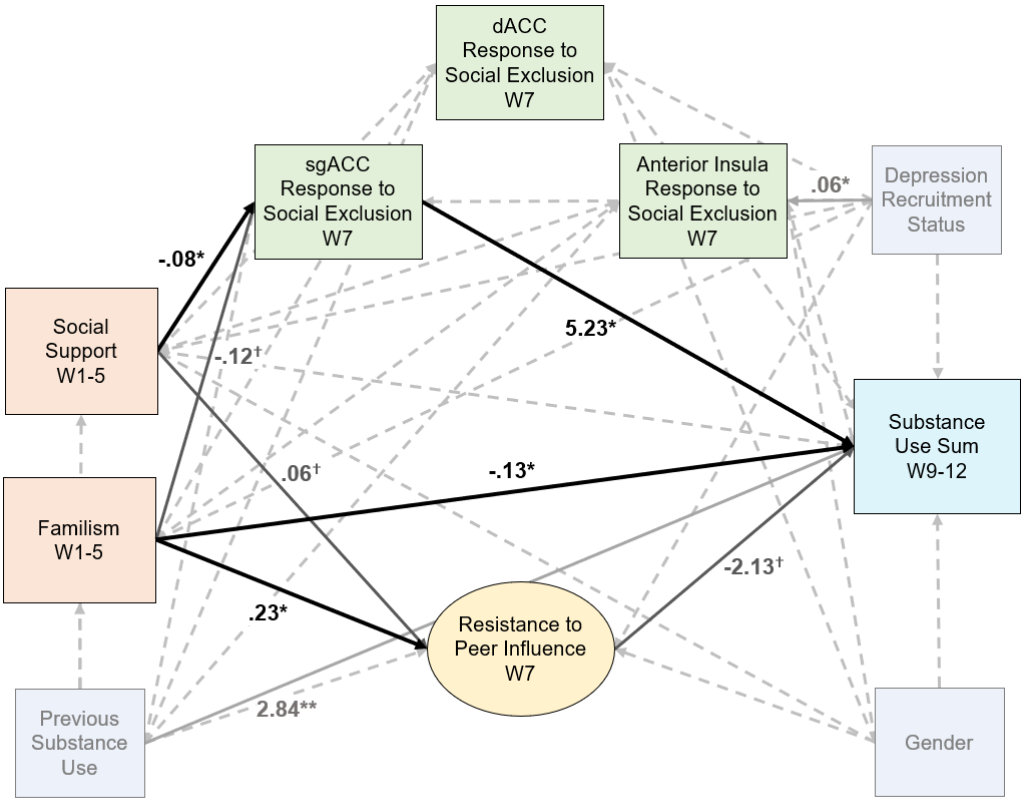
Path Analyses with Social Support and Familism Uniquely Predicting Substance Use

			Regressions			Model Fit				
Model	Outcome	Predictor	*beta*	*SE*	*z*	X^2	CFI	TLI	RMSEA	SRMR
Social Support W1-5 & Substance Use W9-12	Substance Use W9-12	Social Support	-.18*	.21	-1.47**	0	1.0	1.0	0	0
		Gender	.28	.13	.22					
		Previous Use	.47**	.40	2.97**					
		Depression Status	.14	.59	.88					
Familism W1-5 & Substance Use W9-12	Substance Use W9-12	Familism	-.31*	.21	-1.51*	0	1.0	1.0	0	0
		Gender	.10	.23	.08					
		Previous Use	.49**	.34	3.31**					
		Depression Status	.14	.59	.88					

Note: $N = 196$. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$. *beta* = standardized regression weights, *SE* = standard error, *z* = z-score, X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, SRMR = Standardized root mean square residual, W1 = Wave 1/age 10, W3 = Wave 3/age 12, W5 = Wave 5/age 14, W7 = Wave 7/age 16, W9 = Wave 9/age 18, W11 = Wave 11/age 21, W12 = Wave 12/age 23, and Depression Status = Depression recruitment status, coded as 0 = Low and 1 = Elevated, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (Watson et al., 1995). Gender is coded as 0 = Women, 1 = Men. Social Support and Familism reflect averages across waves 1, 3, and 5. Substance Use reflects an average of waves 9, 11, and 12 with cigarettes, cannabis, beer, wine, liquor, and binge drinking.

Figure 3.9

Structural Equation Model with Social Support and Familism Predicting Substance Use Mediated by Resistance to Peer Influence and Neural Response to Social Exclusion



Fit: $X^2(91) = 132.21$, $p < .01$, CFI = .83, TLI = .76, RMSEA = .05, 90% CI [.03, .07], SRMR = .06.

Note: $N = 196$. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$. sgACC = Subgenual anterior cingulate cortex, dACC = Dorsal anterior cingulate cortex, AI = Anterior insula, X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, SRMR = Standardized root mean square residual, W1 = Wave 1/age 10, W3 = Wave 3/age 12, W5 = Wave 5/age 14, W7 = Wave 7/age 16, W9 = Wave 9/age 18, W11 = Wave 11/age 21, W12 = Wave 12/age 23, and Depression Recruitment Status = Depression recruitment status, coded as 0 = Low and 1 = Elevated, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (Watson et al., 1995). Gender is coded as 0 = Women, 1 = Men. Social Support and Familism reflect averages across waves 1, 3, and 5. Substance Use Sum reflects an average of waves 9, 11, and 12 with cigarettes, cannabis, beer, wine, liquor, and binge drinking. Resistance to Peer Influence is latent with 8 questions. Standardized estimates presented. Non-significant paths represented by dashed lines. Indicators of latent factors omitted for clarity.

Table 3.7

Structural Equation Models with Social Support and Familism Uniquely Predicting Substance Use Mediated by Resistance to Peer Influence and Neural Response to Social Exclusion

			Regressions			Model Fit				
Model	Outcome	Predictor	*beta*	*SE*	*z*	X^2	CFI	TLI	RMSEA	SRMR
Social Support W1-5 & Substance Use W9-12						124.36***	.82	.75	.06	.06
	Substance Use W9-12	Social Support	-.62	.95	-.65					
		RPI	-2.92	1.52	-1.58					
		sgACC	6.05*	2.55	2.05*					
		dACC	-2.75	2.07	-.90					
		AI	3.85	2.51	1.51					
		Gender	1.05	1.01	1.08					
		Previous Use	2.39*	1.29	2.48*					
		Depression Status	1.69	1.41	1.11					
	Resistance to Peer Influence W7	Social Support	.08	.05	.88					
		Gender	-.05	.06	-.93					
		Previous Use	-.07	.06	-1.02					
		Depression Status	.06	.07	.84					
	sgACC Response to Social Exclusion W7	Social Support	-.05	.02	-1.28					
		Gender	-.01	.02	-.23					
		Previous Use	.02	.03	.73					
		Depression Status	.01	.03	.22					
	dACC Response to Social Exclusion W7	Social Support	-.03	.02	-1.08					
		Gender	.01	.02	.18					
		Previous Use	-.02	.02	-.67					
		Depression Status	.01	.03	.20					
	AI Response to Social Exclusion W7	Social Support	-.01	.02	-.51					
		Gender	.04	.02	1.20					
		Previous Use	.03	.02	.87					
		Depression Status	.06	.03	1.07					
Familism W1-5 & Substance Use W9-12						127.99***	.81	.74	.06	.07
	Substance Use W9-12	Familism	-1.83	1.68	-1.09					
		RPI	-3.11	1.87	-1.63					
		sgACC	4.15	2.56	1.63					
		dACC	-3.04	2.06	-.99					
		AI	5.91	2.94	2.01					
		Gender	.97	.98	.99					
		Previous Use	1.09*	1.01	1.08*					
		Depression Status	.91	1.24	.78					
	Resistance to Peer Influence W7	Familism	.28*	.10	1.77*					
		Gender	-.04	.06	-.77					
		Previous Use	-.07	.06	-1.19					
		Depression Status	.05	.07	.75					
	sgACC Response to Social Exclusion W7	Familism	-.03	.05	-.27					
		Gender	.01	.03	.17					
		Previous Use	.03	.03	.99					
		Depression Status	.01	.04	.01					
	dACC Response to Social Exclusion	Familism	.06	.04	1.37					
		Gender	.03	.02	1.04					

W7	Previous Use	-.01	.03	-.23
	Depression Status	.04	.03	.02
AI Response to Social Exclusion W7	Familism	.01	.04	.17
	Gender	.04	.03	1.68
	Previous Use	.03	.03	.11
	Depression Status	.06*	.03	2.03*

Note: N = 196. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$. sgACC = Subgenual anterior cingulate cortex, dACC = Dorsal anterior cingulate cortex, AI = Anterior insula, RPI = Resistance to Peer Influence, *beta* = standardized regression weights, *SE* = Standard error, *z* = z-score, X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, and SRMR = Standardized root mean square residual, W1 = Wave 1/age 10, W3 = Wave 3/age 12, W5 = Wave 5/age 14, W7 = Wave 7/age 16, W9 = Wave 9/age 18, W11 = Wave 11/age 21, W12 = Wave 12/age 23, and Depression Status = Depression recruitment status, coded as 0 = Low and 1 = Elevated, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (Watson et al., 1995). Gender is coded as 0 = Women, 1 = Men. Social Support and Familism reflect averages across waves 1, 3, and 5. Substance Use reflects an average of waves 9, 11, and 12 with cigarettes, cannabis, beer, wine, liquor, and binge drinking. Indicators of latent factors omitted for clarity.

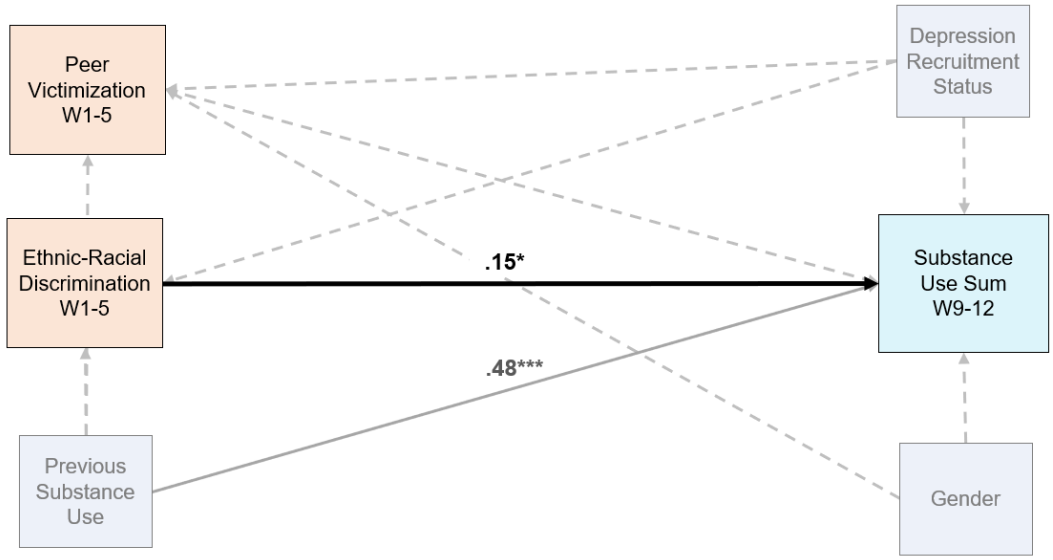
Social Stress, Brain Activity during Exclusion, and Substance Use

In the path analysis, ethnic-racial discrimination across late childhood and early adolescence was positively associated with later substance use across young adulthood (Figure 3.10). When examining each predictor separately, ethnic-racial discrimination predicted substance use, but peer victimization was not significantly associated with use (Table 3.8). In the SEM with mediators RPI and neural response to social exclusion (in the sgACC, dACC, and AI), ethnic-racial discrimination and sgACC activity during social exclusion were positively associated with substance use (Figure 3.11). Additionally, greater peer victimization was associated with lower RPI (i.e., higher susceptibility to peer influence), and adolescents with a higher risk of developing depression demonstrated greater AI response to social exclusion. Other paths, however, were not statistically significant.

When examining peer victimization alone (i.e., removing ethnic-racial discrimination from the model), results were similar (Table 3.9). Victimization predicted RPI, depression recruitment status predicted AI activity during exclusion, and sgACC activity during exclusion predicted substance use. When assessing ethnic-racial discrimination alone, substance use was positively associated with greater ethnic-racial discrimination and greater sgACC response to exclusion; but discrimination was not associated with sgACC activity. In sum, ethnic-racial discrimination (but not peer victimization) during late childhood and early adolescence predicted later substance use in young adulthood, but this effect was not mediated by neural response to social exclusion or self-reported RPI.

Figure 3.10

Path Model with Peer Victimization and Ethnic-Racial Discrimination Predicting Substance Use



Note: $N = 196$. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$. X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, SRMR = Standardized root mean square residual, W1 = Wave 1/age 10, W3 = Wave 3/age 12, W5 = Wave 5/age 14, W7 = Wave 7/age 16, W9 = Wave 9/age 18, W11 = Wave 11/age 21, W12 = Wave 12/age 23, and Depression Recruitment Status = Depression recruitment status, coded as 0 = Low and 1 = Elevated, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (Watson et al., 1995). Gender is coded as 0 = Women, 1 = Men. Peer Victimization and Ethnic-Racial Discrimination reflect averages across waves 1, 3, and 5. Substance Use Sum reflects an average of waves 9, 11, and 12 with cigarettes, cannabis, beer, wine, liquor, and binge drinking.

Table 3.8

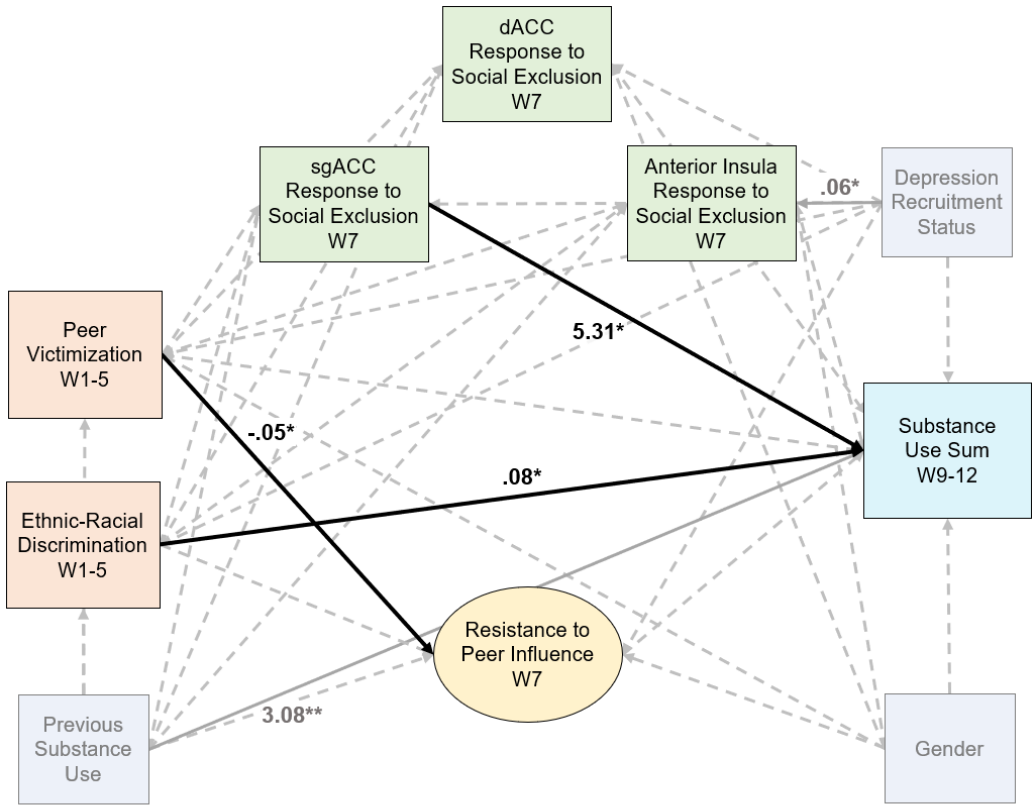
Path Analyses with Peer Victimization and Ethnic-Racial Discrimination Uniquely Predicting Substance Use

			Regressions			Model Fit				
Model	Outcome	Predictor	*beta*	*SE*	*z*	X^2	CFI	TLI	RMSEA	SRMR
Peer Victimization W1-5 & Substance Use W9-12	Substance Use W9-12	Peer Victimization	.23	.21	.35	0	1.0	1.0	0	0
		Gender	.28	.13	.22					
		Previous Use	.47**	.40	2.97**					
		Depression Status	.12	.59	.88					
Ethnic-Racial Discrimination W1-5 & Substance Use W9-12	Substance Use W9-12	Ethnic-Racial Discrimination	-.19*	.21	-1.51*	0	1.0	1.0	0	0
		Gender	.10	.23	.08					
		Previous Use	.49***	.34	3.31**					
		Depression Status	.12	.59	.88					

Note: N = 196. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$. *beta* = standardized regression weights, *SE* = standard error, *z* = z-score, X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, SRMR = Standardized root mean square residual, W1 = Wave 1/age 10, W3 = Wave 3/age 12, W5 = Wave 5/age 14, W7 = Wave 7/age 16, W9 = Wave 9/age 18, W11 = Wave 11/age 21, W12 = Wave 12/age 23, and Depression Status = Depression recruitment status, coded as 0 = Low and 1 = Elevated, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (Watson et al., 1995). Gender is coded as 0 = Women, 1 = Men. Peer Victimization and Ethnic-Racial Discrimination reflect averages across waves 1, 3, and 5. Substance Use reflects an average of waves 9, 11, and 12 with cigarettes, cannabis, beer, wine, liquor, and binge drinking.

Figure 3.11

Structural Equation Model with Peer Victimization and Ethnic-Racial Discrimination Predicting Substance Use Mediated by Resistance to Peer Influence and Neural Response to Social Exclusion



Note: N = 196. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$. sgACC = Subgenual anterior cingulate cortex, dACC = Dorsal anterior cingulate cortex, AI = Anterior insula, X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, SRMR = Standardized root mean square residual, W1 = Wave 1/age 10, W3 = Wave 3/age 12, W5 = Wave 5/age 14, W7 = Wave 7/age 16, W9 = Wave 9/age 18, W11 = Wave 11/age 21, W12 = Wave 12/age 23, and Depression Recruitment Status = Depression recruitment status, coded as 0 = Low and 1 = Elevated, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (Watson et al., 1995). Gender is coded as 0 = Women, 1 = Men. Peer Victimization and Ethnic-Racial Discrimination reflect averages across waves 1, 3, and 5. Substance Use Sum reflects an average of waves 9, 11, and 12 with cigarettes, cannabis, beer, wine, liquor, and binge drinking. Resistance to Peer Influence is latent with 8 questions.

Standardized estimates presented. Non-significant paths represented by dashed lines. Indicators of latent factors omitted for clarity.

Table 3.9

Structural Equation Models Peer Victimization and Ethnic-Racial Discrimination Uniquely Predicting Substance Use Mediated by Resistance to Peer Influence and Neural Response to Social Exclusion

			Regressions			Model Fit				
Model	Outcome	Predictor	*beta*	*SE*	*z*	X^2	CFI	TLI	RMSEA	SRMR
Peer Victimization W1-5 & Substance Use W9-12	Substance Use W9-12	Peer Victimization	.02	.06	.25	131.73**	.82	.76	.06	.07
		RPI	-.81	.85	-1.22					
		sgACC	6.12*	1.55	2.07*					
		dACC	-2.59	2.81	-.05					
		AI	4.00	3.01	1.14					
		Gender	.10	.29	.01					
		Previous Use	3.08**	1.01	1.26*					
		Depression Status	.38	1.61	.85					
	Resistance to Peer Influence W7	Peer Victimization	-.09*	.01	-1.63*					
		Gender	-.06	.06	-1.04					
		Previous Use	-.09	.06	-1.41					
		Depression Status	.05	.07	.83					
	sgACC Response to Social Exclusion W7	Peer Victimization	-.02	.02	-1.07					
		Gender	.04	.03	1.55					
		Previous Use	-.01	.03	-.10					
		Depression Status	.00	.04	.01					
	dACC Response to Social Exclusion W7	Peer Victimization	-.01	.01	-.05					
		Gender	.03	.02	1.14					
		Previous Use	.01	.03	.01					
		Depression Status	.01	.03	.16					
	AI Response to Social Exclusion W7	Peer Victimization	.01	.02	.72					
		Gender	.01	.03	.23					
		Previous Use	.03	.03	.93					
		Depression Status	.06*	.03	1.99*					
Ethnic-Racial Discrimination W1-5 & Substance Use W9-12	Substance Use W9-12	Ethnic-Racial Discrimination	.11*	.09	1.40*	130.12**	.86	.78	.05	.06
		RPI	-.37	.22	-1.01					
		sgACC	2.52	1.98	.66					
		dACC	2.31	2.01	.98					
		AI	4.01	2.98	1.16					
		Gender	.10	.29	.01					
		Previous Use	3.08**	1.01	1.26*					
		Depression Status	1.21	1.64	.73					
	Resistance to Peer Influence W7	Ethnic-Racial Discrimination	-.13	.17	.86					

	Gender	-.06	.06	-1.04
	Previous Use	-.09	.06	-1.41
	Depression Status	.06	.07	.77
sgACC Response to Social Exclusion W7	Ethnic-Racial Discrimination	.12	.08	1.51
	Gender	.04	.03	1.55
	Previous Use	-.01	.03	-.10
	Depression Status	.01	.03	.17
dACC Response to Social Exclusion W7	Ethnic-Racial Discrimination	.04	.07	.53
	Gender	.03	.02	1.14
	Previous Use	.01	.03	.01
	Depression Status	.00	.03	.11
AI Response to Social Exclusion W7	Ethnic-Racial Discrimination	.01	.07	.12
	Gender	.01	.03	.23
	Previous Use	.03	.03	.93
	Depression Status	.06*	.03	2.00*

Note: N = 196. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$. sgACC = Subgenual anterior cingulate cortex, dACC = Dorsal anterior cingulate cortex, AI = Anterior insula, RPI = Resistance to Peer Influence, *beta* = standardized regression weights, *SE* = Standard error, *z* = z-score, X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, and SRMR = Standardized root mean square residual, W1 = Wave 1/age 10, W3 = Wave 3/age 12, W5 = Wave 5/age 14, W7 = Wave 7/age 16, W9 = Wave 9/age 18, W11 = Wave 11/age 21, W12 = Wave 12/age 23, and Depression Status = Depression recruitment status, coded as 0 = Low and 1 = Elevated, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (Watson et al., 1995). Gender is coded as 0 = Women, 1 = Men. Peer Victimization and Ethnic-Racial Discrimination reflect averages across waves 1, 3, and 5. Substance Use reflects an average of waves 9, 11, and 12 with cigarettes, cannabis, beer, wine, liquor, and binge drinking. Indicators of latent factors omitted for clarity.

Early Substance Use, Brain Activity during Exclusion, and Later Social Functioning

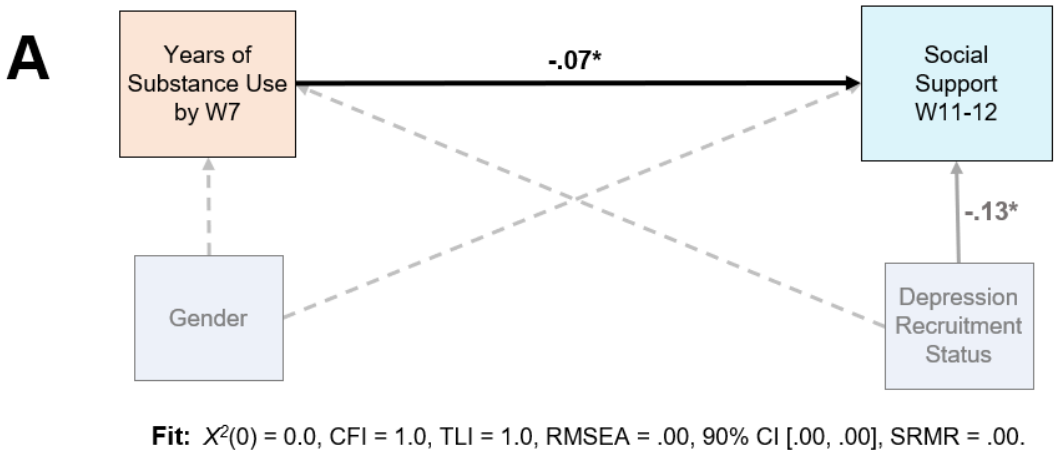
To address hypotheses about earlier substance use influencing later social functioning, analyses included SEMs with the predictor as number of years of substance use by wave 7/age 16 (calculated by subtracting age of first substance use from age at wave 7) and outcomes as social support averaged across waves 11/age 21 and 12/age 23 (given that the measure for social support changed significantly between waves 9 and 11; see Method), latent prosocial behaviors at wave 9/age 18, and quality of romantic relationship averaged across waves 9/age 18 and 11/age 21. In the SEMS with only predictors (i.e., no mediators), years of substance use was negatively associated with social support (Figure 3.10A) and prosocial behaviors (Figure 3.10B). Young adults with a high risk of depression during adolescence reported less social support during young adulthood (Figure 3.10A). Romantic relationship quality, however, was not significantly associated with early substance use (Table 3.10). Women reported higher relationship quality than men.

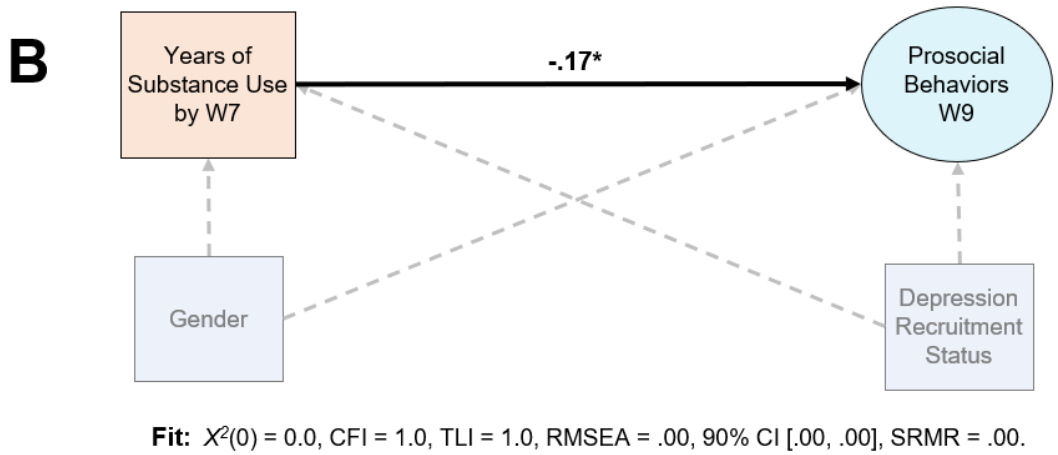
In the SEMs with mediators RPI and neural response to social exclusion (in the sgACC, dACC, and AI), social support was negatively associated with years of substance use, and positively related with RPI (Figure 3.11). A higher number of years of substance use predicted less dACC activity during social exclusion. Years of substance use was not significantly associated with RPI. Prosocial behaviors were negatively related with years of substance use (Figure 3.12). Neural activity did not predict prosocial behaviors, contrary to what preliminary correlations suggested; and RPI also did not predict prosocial behaviors. Romantic relationship quality was not significantly associated with years of substance use, RPI, or neural activity during social exclusion (Table 3.11). Depression risk status was negatively associated with romantic relationship quality (i.e., those with a high risk reported lower-quality relationships),

and positively associated with AI response to social exclusion. Years of substance use was also negatively associated with dACC response to exclusion in this model. In sum, earlier substance use predicts lower social support and prosocial behaviors, but not relationship quality; and neural activity and RPI did not mediate the links between substance use and social support and prosocial behaviors.

Figure 3.12

Path Models with Years of Substance Use Predicting Social Support and Prosocial Behaviors





Note: $N = 196$. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$. X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, SRMR = Standardized root mean square residual, W7 = Wave 7/age 16, W9 = Wave 9/age 18, W11 = Wave 11/age 21, W12 = Wave 12/age 23, and Depression Recruitment Status = Depression recruitment status, coded as 0 = Low and 1 = Elevated, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (Watson et al., 1995). Panel A reflects social support as the outcome, whereas Panel B reflects prosocial behaviors as the outcome. Gender is coded as 0 = Women, 1 = Men. Years of Substance Use was calculated by subtracting age of first substance use from current age at Wave 7. Social Support reflects an average of waves 11 and 12 (instead of 9 and 11) due to a significant change in the questionnaire. Standardized estimates presented. Non-significant paths represented by dashed lines. Indicators of latent factors omitted for clarity.

Table 3.10

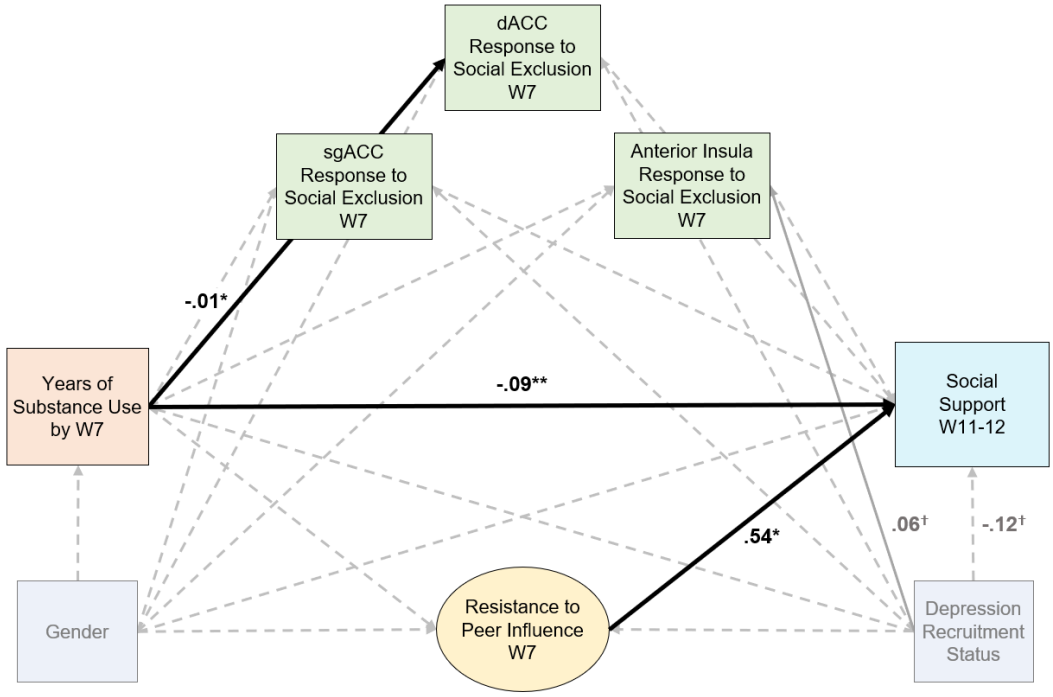
Path Analysis with Years of Substance Use Predicting Romantic Relationship Quality

			Regressions			Model Fit				
Model	Outcome	Predictor	*beta*	*SE*	*z*	X^2	CFI	TLI	RMSEA	SRMR
Years of Substance Use by W7 & Relationship Quality W9-11	Relationship Quality W9-11	Years of Use	-.02	.02	-.46	0	1.0	1.0	0	0
		Gender	-.59*	.07	-2.02*					
		Depression Status	-.23†	.09	-1.58†					

Note: N = 94. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$. *beta* = standardized regression weights, *SE* = Standard error, *z* = z-score, X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, SRMR = Standardized root mean square residual, W7 = Wave 7/age 16, W9 = Wave 9/age 18, W11 = Wave 11/age 21, and Depression Status = Depression recruitment status, coded as 0 = Low and 1 = Elevated, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (Watson et al., 1995). Gender is coded as 0 = Women, 1 = Men. Relationship Quality reflects an average across waves 9 and 11. Years of Use was calculated by subtracting age of first substance use from current age at Wave 7.

Figure 3.13

Structural Equation Model with Years of Substance Use Predicting Social Support Mediated by Resistance to Peer Influence and Neural Response to Social Exclusion



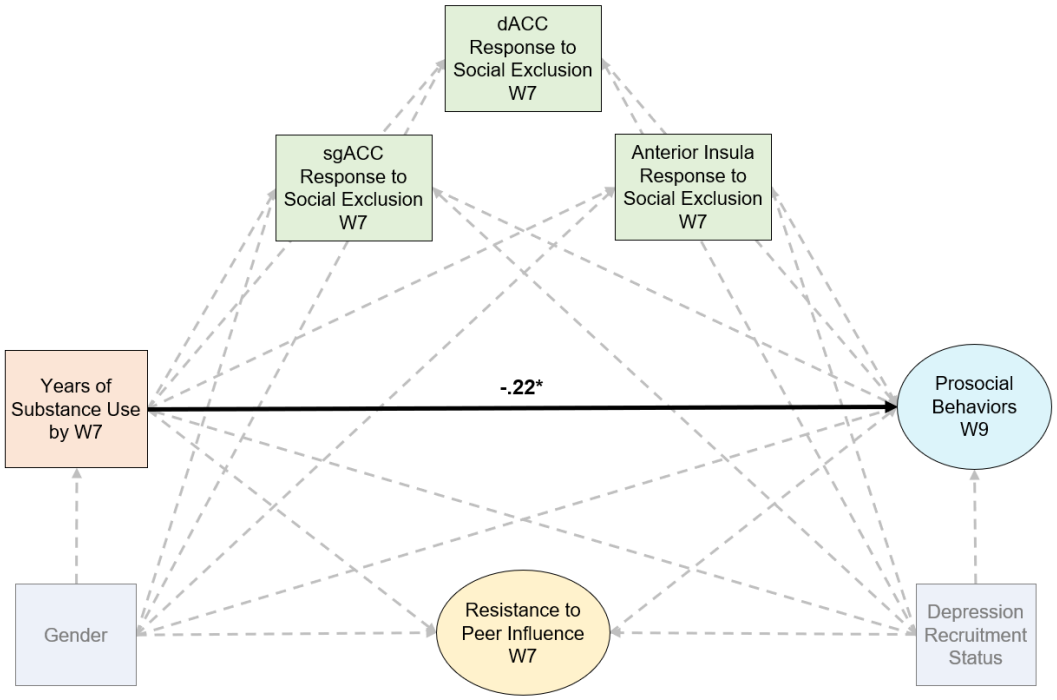
Fit: $X^2(75) = 122.01$, $p < .001$, CFI = .79, TLI = .71, RMSEA = .07, 90% CI [.04, .09], SRMR = .07.

Note: $N = 196$. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$. sgACC = Subgenual anterior cingulate cortex, dACC = Dorsal anterior cingulate cortex, AI = Anterior insula, X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, SRMR = Standardized root mean square residual, W1 = Wave 1/age 10, W3 = Wave 3/age 12, W5 = Wave 5/age 14, W7 = Wave 7/age 16, W9 = Wave 9/age 18, W11 = Wave 11/age 21, and Depression Recruitment Status = Depression recruitment status, coded as 0 = Low and 1 = Elevated, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (Watson et al., 1995). Gender is coded as 0 = Women, 1 = Men. Years of Substance Use was calculated by subtracting age of first substance use from current age at Wave 7. Social Support reflects an average of waves 11 and 12 (instead of 9 and 11) due to a significant change in the questionnaire. Resistance to Peer Influence is latent with 8 questions. Standardized estimates presented. Non-significant paths represented by dashed lines. Indicators of latent factors omitted for clarity.

Figure 3.14

Structural Equation Model with Years of Substance Use Predicting Prosocial Behaviors

Mediated by Resistance to Peer Influence and Neural Response to Social Exclusion



Fit: $X^2(75) = 111.73$, $p < .01$, CFI = .76, TLI = .69, RMSEA = .07, 90% CI [.04, .09], SRMR = .08.

Note: $N = 196$. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$. sgACC = Subgenual anterior cingulate cortex, dACC = Dorsal anterior cingulate cortex, AI = Anterior insula, X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, SRMR = Standardized root mean square residual. W1 = Wave 1/age 10, W3 = Wave 3/age 12, W5 = Wave 5/age 14, W7 = Wave 7/age 16, W9 = Wave 9/age 18, W11 = Wave 11/age 21, and Depression Recruitment Status = Depression recruitment status, coded as 0 = Low and 1 = Elevated, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (Watson et al., 1995). Gender is coded as 0 = Women, 1 = Men. Years of Substance Use was calculated by subtracting age of first substance use from current age at Wave 7. Resistance to Peer Influence is latent with 8 questions, and Prosocial Behaviors is latent with 5 questions. Standardized estimates presented. Non-significant paths represented by dashed lines. Indicators of latent factors omitted for clarity.

Table 3.11

Structural Equation Model with Years of Substance Use Predicting Romantic Relationship Quality Mediated by Resistance to Peer Influence and Neural Response to Social Exclusion

			Regressions			Model Fit				
Model	Outcome	Predictor	*beta*	*SE*	*z*	X^2	CFI	TLI	RMSEA	SRMR
Years of Substance Use by W7 & Relationship Quality W9-11						110.64**	.85	.79	.06	.07
	Relationship Quality W9-11	Years of Use	-.04†	.02	-1.65†					
		RPI	.21†	.12	1.70†					
		sgACC	.12	.19	.60					
		dACC	-.32	.24	-1.33					
		AI	.08	.22	.36					
		Gender	-.09	.07	-1.19					
		Depression Status	.24**	.09	2.70**					
	Resistance to Peer Influence W7	Years of Use	.03	.02	1.64					
		Gender	-.04	.07	-.52					
		Depression Status	-.01	.08	-.13					
	sgACC Response to Social Exclusion W7	Years of Use	-.01	.01	-.84					
		Gender	-.02	.03	-.60					
		Depression Status	.03	.04	.83					
	dACC Response to Social Exclusion W7	Years of Use	-.30*	.01	-2.13*					
		Gender	.00	.03	.10					
		Depression Status	-.01	.03	-.36					
	AI Response to Social Exclusion W7	Years of Use	.01	.01	.78					
		Gender	.07	.03	1.01					
		Depression Status	-.07*	.04	-2.05*					

Note: N = 94. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$. sgACC = Subgenual anterior cingulate cortex, dACC = Dorsal anterior cingulate cortex, AI = Anterior insula, RPI = Resistance to Peer Influence, *beta* = standardized regression weights, *SE* = Standard error, *z* = z-score, X^2 = Chi-square goodness-of-fit, CFI = Comparative fit index, TLI = Tucker Lewis index, RMSEA = Root mean square error of approximation, CI = Confidence interval, SRMR = Standardized root mean square residual, W9 = Wave 9/age 18, W11 = Wave 11/age 21, and Depression Status = Depression recruitment status, coded as 0 = Low and 1 = Elevated, representing the risk of depression based on self-reported symptoms in ninth grade (age 14-15 years) from the computerized Diagnostic Interview Schedule for Children-IV (Shaffer et al., 2000), and General Distress and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire (Watson et al., 1995). Gender is coded as 0 = Women, 1 = Men. Relationship Quality reflects an average across waves 9 and 11. Years of Use was calculated by subtracting age of first substance use from current age at Wave 7. RPI is latent with 8 questions.

Discussion

The current study investigated substance use in adolescence and young adulthood as it relates to social functioning over time, and whether adolescent neural activity during an instance of social exclusion – as well as self-reported resistance to peer influence (RPI) – mediated these associations. Analyses compared early experiences of social support and stress on later substance use with early experiences of substance use on later social functioning. This study is the first to directly compare both possible pathways; and the first to contextualize different developmental theories by extending concepts of adolescent risk-taking, testing bidirectional connections over time, and informing how these processes occur in diverse populations as this study involved Mexican-origin adolescents. One set of hypotheses focused on early social experiences and later substance use, which included that (1) more social support (social support, familism) in late childhood/early adolescence would predict less substance use in young adulthood, (2) more social stress (peer victimization, ethnic-racial discrimination) would predict more use, (3) neural activity during social exclusion and would mediate paths between early support and later use, (4) neural activity would mediate the paths between early stress and later use, (5) RPI would also mediate links between support and substance use, and (6) RPI would mediate links between early stress and later substance use. Another set of hypotheses centered on early substance use and later social functioning, which included that (7) earlier substance use would predict worse social functioning in young adulthood, including less social support, less prosocial behaviors, and lower romantic relationship quality, (8) neural activity during social exclusion and would mediate relations among early use and later functioning, and lastly, (9) RPI would mediate relations among early use and later functioning. Hypotheses were partially supported.

Early experiences of social support from peers and family and high endorsement of familism values during childhood and early adolescence resulted in less self-reported substance use during young adulthood. These findings align with previous work suggesting that high social support during adolescence is associated with less substance use concurrently and over time (Ennett et al., 2008; Heerde & Hemphill, 2018), and that higher endorsement of familism is also associated with less use (Lardier et al., 2018). The current study, however, assessed peer and family support together, due to a methodological change in the support measure during young adulthood. In past studies separating the two sources of support, there is evidence that parental support is protective (Hummel et al., 2013; LaFreniere et al., 2022; Mills et al., 2021), but peer support can be either protective (Forster et al., 2015; Gliksberg et al., 2021; Stewart et al., 2022) or harmful in increasing substance use (Gázquez et al., 2016; Piko, 2000; Wills et al., 2004).

The present study also found that neural response to social exclusion in the sgACC only partially mediated the link between early social support and later substance use. Social support was negatively associated with sgACC activity, which in turn was positively associated with substance use; but both the indirect effect and Sobel's test suggested no full mediation effect. RPI was not a secondary mediator, as it was related to familism consistently but not to social support or substance use. The lack of a significant association between RPI and substance use was surprising, given that past work has reported higher substance use in youth who endorse lower RPI (Monahan et al., 2009). One possible explanation is that RPI was relatively high in the current study's sample, with limited variability across participants.

Partial support was found for predictions about early social stressors contributing to later substance use. A history of experiencing discrimination from peers based on ethnicity and/or race from childhood through early adolescence predicted more substance use in young

adulthood; and this effect was specific to ethnic-racial discrimination, as a history of being victimized more generally (e.g., being left out of activities) by peers was not associated with later substance use. Past work has identified a consistent link between discrimination and substance use, in both adolescents and adults (Baiden et al., 2023; Cave et al., 2020; Cénat et al., 2023; Pachter et al., 2018; Sanderson et al., 2020; Sapouna et al., 2023). Latinx adolescents experience more discrimination and peer victimization from peers (Hong et al., 2014; Sawyer et al., 2008; Vitoroulis & Georgiades, 2017), but the sample studied in this investigation reported low scores on these experiences across late childhood and early adolescence, leading to a restriction of range in responses. Regarding ethnic-racial discrimination, it is plausible that adolescents in the CFP faced less discrimination due to northern California having a higher amount of individuals from Latinx populations than other states in the U.S., where discrimination might be more common. Relatedly, these adolescents likely attended more racially diverse schools, creating opportunities for more inclusive environments (Nishina et al., 2019) and a higher sense of school belonging (Lewis et al., 2017). Regarding peer victimization, many studies have reported significant associations with substance use (Hertz et al., 2015; Hong et al., 2022; King et al., 2014; Tretyak et al., 2022), but some studies have reported null or negative effects (Kaltiala-Heino et al., 2000; Nansel et al., 2001; Vannucci et al., 2021). The current study's results, however, could be a consequence of restricted range and not a lack of victimization effects. Contrary to predictions, neural response to social exclusion and RPI were not significantly associated with peer victimization or ethnic-racial discrimination.

Adolescents with a history of earlier substance use (beginning between the ages of 10 and 14) reported experiencing less social support from friends and family later on in young adulthood, in support of hypotheses. The literature on this topic is small, but suggests that early

substance use has negative consequences for future social functioning (Clay & Parker, 2018), and that adults who heavily use substances often have difficulty maintaining healthy social relationships (Sinha, 2008). The present findings support the idea that earlier onset can hinder friendships and other aspects of social functioning, even into young adulthood. Results also suggested that more RPI predicted more social support, but early substance use was not associated with RPI or neural activity, suggesting no mediating effects. Thus, RPI was associated with social support both early in adolescence and later in young adulthood, but not consistently with social stressors.

Earlier onset of substance use predicted lower levels of prosocial behavior during young adulthood, in support of hypotheses. This finding is consistent with past work that has found prospective effects (Davis et al., 2017) and concurrent effects between prosocial behavior and substance use (Frobel et al., 2022). For example, Davis et al. (2017) found that early use of substances was linked with less prosocial behaviors in young women in college. In the current study, prosocial behavior was not linked to neural response to social exclusion or self-reported RPI in the SEMs, which was surprising given that preliminary correlations suggested associations between prosocial behaviors and these variables. It is possible that the sample size, although large, was not sufficient to capture these patterns in the complex models. Future work should rely upon larger samples to test associations among prosocial behaviors, RPI, and neural activity during social exclusion.

For romantic relationships, women reported being in higher-quality relationships than men, and individuals with a high risk for depression during early adolescence reported lower relationship quality during young adulthood. No other significant effects emerged among relationship quality, history of substance use, RPI, or neural activity during social exclusion;

however, this is likely due to a small sample size. Only 94 participants reported being in a romantic relationship at age 21, and only 85 at age 18, reducing the ability to analyze and interpret complex models. Bivariate correlations suggested that romantic relationship quality was negatively associated with substance use during young adulthood (i.e., concurrently), and positively associated with social support and familism during early adolescence (i.e., prospectively). Neural activity while being excluded during adolescence was not associated with relationship quality. With a larger sample, participants could be categorized by relationship status, and multi-group analyses could be explored. Given the relevance of romantic relationships during adolescence and young adulthood, future studies can further probe the associations among neural activity, substance use, and quality of romantic relationships.

The present study involves some limitations. First, the measures used to capture social experiences and functioning showed little variability over time, and certain measures had a restricted range of responses and low variability. For example, adolescents overall reported low amounts of peer victimization and ethnic-racial discrimination, and high amounts of social support and familism. Victimization in particular was very low, which could have driven a lack of associations with brain activity and substance use. Second, claims about directionality of effects are hindered by differences in the conceptualization of social stress between late childhood and young adulthood. Although it was fortunate to have the same measure of social support during both childhood and adulthood, there were no explicit measures of social stress for young adults that could be compared directly to earlier experiences of social stress. Prosocial behaviors reflect overall social functioning, but it would be preferable to have clear experiences of social stress, such as being rejected by coworkers or potential romantic partners. Third, assessing romantic relationship quality limited the sample size to a small number of young adults

who reported being in an established relationship, whereas a more general questionnaire about dating experiences could reveal that the way in which young adults process and respond to social exclusion explains subsequent substance use patterns. Lastly, data were not collected about adolescents' social use of substances, such as behaviors within specific social situations or perceptions of friends' behaviors. Given that adolescents and young adults typically experiment with friends and other peers, disentangling solitary and social use would provide additional insight. For example, an adolescent's responses might differ between the questions, "*How often have you drank beer in the past 3 months*?" and "*How often have you drank beer with your friends in the past 3 months?*" Another interesting avenue would be to compare Cyberball to other social exclusion tasks. Future work could capture social aspects of substance use, and rely upon different indices of social rejection.

Overall, the current study was the first to assess the bidirectional associations between substance use and social functioning from early adolescence to young adulthood, considering neural response to social exclusion and self-reported resistance to peer influence as mediators. Adolescence is a developmental period where peers become increasingly influential, but social support from parents and other family members still protects against substance use risk, especially in Mexican-origin individuals that endorse high levels of familism (Lardier et al., 2018; Telzer et al., 2013). Social stressors are highly salient during adolescence, but individual variability exists in how individuals process and react to stressful social situations. The present study revealed that early experiences of social support from friends and family were protective against later substance use, and that sgACC activity during social exclusion partially mediated this link. Endorsing a high level of familism also predicted higher RPI during adolescence, and lower substance use during young adulthood. Results also indicated that early ethnic-racial

discrimination led to increased substance use in this sample of Mexican-origin individuals, but more general peer victimization did not. Earlier use of substances was associated with reporting less social support in adulthood, and less prosocial behavior; but early use was not related to romantic relationship quality in the small subsample of young adults in committed relationships. As a whole, the findings from this study provide novel insight into the directionality of effects between social functioning and substance use, and the role of the adolescent brain's reaction to stressful social experiences. Social processes remain crucial to consider in understanding, and hopefully preventing, substance use and its negative effects on development.

CHAPTER FOUR

GENERAL CONCLUSION

Substance use is a pressing public health concern, and disproportionately impacts Latinx populations in the U.S. (Cruz et al., 2019; Miech et al., 2024). Latinx adolescents tend to have an earlier onset of use (Trent et al., 2023), raising the risk of negative impacts on the brain (Lees et al., 2020) and social functioning in adulthood (Sinha, 2008). Past developmental neuroscience work has associated neural activity during monetary reward tasks with substance use, including both low (Büchel et al., 2017) and high activity (Tervo-Clemmens et al., 2020). Much less is known, however, about sensitivity to social rewards and other types of experiences, such as social exclusion. Additionally, social context has seldom been considered, despite the inherently social nature of substance use (Teunissen et al., 2012) and the predictive power of early social experiences (McCollum et al., 2023). Substance use has been associated negatively with early social support (S. Fisher et al., 2019), positively with racial/ethnic discrimination (Baiden et al., 2023), and to a lesser extent, positively with victimization by peers (Tretyak et al., 2022). Still, no studies to my knowledge have incorporated brain function into these complex pathways, as highlighted in my review paper (Beard et al., 2022b). My dissertation addressed these gaps in the literature and contextualized developmental theories, including the Social Plasticity Hypothesis of substance use desistance during young adulthood (Cousijn et al., 2017), the Triadic Model of motivated behavior (Ernst & Fudge, 2009), and Dual-Systems models of adolescent risk-taking (Shulman et al., 2016). Study 1 also incorporated the Impulsivity (Buckholtz et al., 2010) and Reward Deficiency (Blum et al., 2000) views of addiction. Findings provide a foundation for future work on social-neurobiological contributors to substance use, and potential interventions that consider brain development and social contexts, especially for Latinx individuals.

Study 1 examined how neural responses to social and monetary rewards were bidirectionally associated with substance use from mid-adolescence to young adulthood, guided by dual-systems models (Shulman et al., 2016) and the social plasticity hypothesis (Cousijn et al., 2017). Analyses involved data from the longitudinal California Families Project (CFP), including neurobiological substudies during which participants completed the Monetary Incentive Delay (MID) and Cyberball (a computerized ball-tossing game) tasks at age 17. Using the contrast of Inclusion > Baseline, social inclusion elicited activity in the NAcc and mPFC similarly to monetary reward anticipation, and mPFC response to this social reward increased by age 19 while NAcc response to monetary reward decreased. NAcc activation to social reward at age 17 was positively associated with change in substance use from ages 18 to 21, such that a larger increase in use was found in adolescents who previously showed more brain activation.

Further, change in NAcc activity during monetary reward was positively associated with change in substance use, such that adolescents who increased in activation reported a steeper increase in substance use by age 21. These links among neural response and substance use were unidirectional, as age 16 substance use did not predict change in brain, and change in use did not predict higher neural response at age 19. In sum, social inclusion activated reward regions of the brain, and mPFC response increased over time; and change in substance use was related with age 17 social inclusion activity as well as change in NAcc response to inclusion over time.

Study 2 investigated whether neural response to social exclusion and self-reported resistance to peer influence (RPI) mediated the associations among early social support/stress and later substance use, as well as early substance use and later social functioning, guided by the social plasticity hypothesis (Cousijn et al., 2017). Compared to the focus of Study 1 on social inclusion, Study 2 tested the contrast of Exclusion > Baseline to characterize how the adolescent

brain processes a stressful social experience. Results suggested that endorsing high familism and perceiving high social support from family and friends during late childhood/early adolescence led to less substance use during young adulthood, and this pathway was partially mediated by sgACC activation to exclusion. RPI was not a secondary mediator, as it was positively associated with familism not associated with substance use or social support. Perceiving high ethnic-racial discrimination predicted more substance use, but this link was not explained by neural activity or RPI. Peer victimization was not significantly related with RPI or neural response.

Regarding later social functioning, earlier onset of substance use corresponded to less perceived social support during young adulthood, as well as less prosocial behavior. Early use was not connected with later romantic relationship quality, although power was limited due to a small subsample of participants being in a relationship. Thus, early social support and familism were protective against substance use, while ethnic-racial discrimination heightened use; but RPI did not mediate these associations, and sgACC response partially mediated in one analysis. Early substance use negatively impacted later social support and prosociality, but with no significant involvement of the brain or self-reported susceptibility to social influence.

Taken together, these studies suggest that neurobiological sensitivity to social rewards and stressors are connected to substance use and social functioning in complex ways over time. Higher neural response to social inclusion during mid-adolescence might be a risk factor for more substance use in adulthood, but higher neural response to social exclusion does not necessarily raise the risk. Early experiences of social support and social stress predicted lower and higher substance use, respectively; and earlier use of substances predicted some aspects of social functioning later on. Rather than brain activity during social exclusion accounting for these links, it is possible that different neural mechanisms play a role instead, such as those

invoked by a task involving discrimination, or a task involving social support. Exploring these longitudinal associations in Mexican-origin adolescents allowed for new insights into how social factors, such as discrimination, and brain function relate in non-WEIRD (Chiao & Cheon, 2010; Burns et al., 2019) samples. Indeed, most previous work – especially neuroscience work – has included participants from WEIRD populations, neglecting unique stressors experienced (e.g., discrimination) as well as unique assets and strengths (e.g., familism). The present dissertation provides valuable information on how some of these factors shape substance use.

Dual-systems models (Shulman et al., 2016) typically focus on domain-general rewards, and empirical investigations have relied on monetary reward (Beard et al., 2022b). Findings from Study 1, however, affirm past work showing that social acceptance is rewarding to adolescents (Flannery et al., 2023; Jarcho et al., 2022) as social inclusion elicited activity in the NAcc and mPFC. As only a few studies have examined social reward response in the context of substance use, the current findings contribute to this growing literature. Considering the social plasticity hypothesis (Cousijn et al., 2018), high neural activity during both inclusion and exclusion might reflect high social attunement, as adolescents are paying close attention to social environments and using information to guide their substance-related decisions. In addition to social inclusion eliciting activity in reward regions, social exclusion elicits activity in regions supporting salience and attention (insula, subgenual ACC) as well as executive control (dACC) (Vijayakumar et al., 2017). As neural systems continue to mature, young adults face transitions in responsibilities and social relationships, such as with coworkers and romantic partners. Continued attunement to social supports and stressors likely plays a role in substance use across adult development. Overall, this dissertation highlights fruitful areas for future research, and further supports efforts

for substance use prevention and intervention in diverse populations with its novel focus on social influences implicated in substance use during adolescence and young adulthood.

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APPENDIX A

Supplementary Materials Used in Both Studies

Supplement A1

Questionnaire Used to Assess Substance Use in Both Study 1 and Study 2

Alcohol, Tobacco, and Other Drug Use (ATOD, 26 items)

DESCRIPTION

This 26-item scale focuses on adolescent's alcohol, tobacco, and other drug use. It includes questions about age at first use, how much alcohol and drugs are used, and the amount of alcohol and drugs used. Items 1 through 9 were developed from a scale by Elliott, Huizinga, & Ageton (1985). The rest of the items were developed from diverse sources by Rand Conger. For items 1 through 9, response options were changed from a 3 point scale to a 4 point scale.

ASSOCIATED PAPERS

Elliott, D.S., Huizinga, D., & Ageton, S.S. (1985) Explaining delinquency and drug use. Beverly Hills, CA; Sage.

Now I would like to know if you have ever done any of the following things. Please answer Yes or No **Ahora quiero saber si has hecho lo siguiente. Por favor contesta Sí o No.**	
	Response Categories
	1 = Yes/ Sí
	2 = No/ No
	3= Not applicable (Not asked at Wave 1 and 2 for Child)
	8 = Refusal
	9 = Don't know
atod01	Have you ever used or tried cigarettes? ¿Alguna vez has usado o probado cigarros?
atod02	Have you ever used or tried beer - more than just a few sips? ¿Alguna vez has usado o probado cerveza - más que unas pruebas?
atod03	Wine, or wine coolers - more than just a few sips? Vino, o 'coolers' - más que unas pruebas?
atod04	Hard liquor such as tequila, whiskey, vodka, gin, or other liquor? Licores fuertes como tequila, 'whiskey', 'vodka', ginebra u otro licor?
atod05	Have you ever used or tried marijuana - also called a jay, or pot, weed, grass, hash, bud? ¿Alguna vez has usado o probado marihuana - también le dicen mota, hierba, la grifa?

atod06	Inhalants - things you sniff or breathe to get high like glue, paint, gasoline, poppers, rush, nitrous gas etc? Inhalantes - esas cosas que uno respira para ponerse 'en onda', así como pegamento, pintura, gasolina, 'poppers' y otras cosas como esas?
atod07	Any other illegal drugs - like cocaine, crack, ecstasy, LSD, speed, heroin, etc? Otras drogas ilegales como cocaína/coca, el crack, alucinógeno éxtasis, asido, anfetaminas, heroína, u otras cosas como estas?
atod08	Have you ever been drunk after drinking alcohol? ¿En alguna ocasión, has estado borracho/a después de tomar alcohol?
atod09	Have you ever been high (loaded, stoned, or wasted) from using drugs? ¿En alguna ocasión, has estado tocado/a (grifo, mafufo, hasta arriba) por haber usado drogas?

Questions atod10 - atod16		
atod10	How old were you when you first tried cigarettes? ¿Cuantos años tenías cuando probaste cigarros por primera vez?	
	__	Answer must range from 2 to 12
	98	Refusal
	99	Don't know
atod11	How old were you when you first tried beer? ¿Cuantos años tenías cuando probaste cerveza por primera vez?	
	__	Answer must range from 2 to 12
	98	Refusal
	99	Don't know
atod12	How old were you when you first tried wine, or wine coolers? ¿Cuantos años tenías cuando probaste vino o 'coolers' por primera vez?	
	__	Answer must range from 2 to 12
	98	Refusal
	99	Don't know
atod13	How old were you when you first tried hard liquor? ¿Cuantos años tenías cuando probaste licores fuertes por primera vez?	
	__	Answer must range from 2 to 12
	98	Refusal
	99	Don't know
atod14	How old were you when you first tried marijuana? ¿Cuantos años tenías cuando probaste marihuana por primera vez?	
	__	Answer must range from 2 to 12
	98	Refusal
	99	Don't know
atod15	How old were you when you first tried inhalants? ¿Cuantos años tenías cuando probaste inhalantes por primera vez?	
	__	Answer must range from 2 to 12

	98	Refusal
	99	Don't know
atod16	How old were you when you first tried these other drugs (cocaine, crack, ecstasy, LSD, speed, heroin, etc.)? ¿Cuantos años tenías cuando probaste estas drogas ilegales por primera vez (cocaína/coca, el crack, alucinógeno éxtasis, asido, anfetaminas, heroína, u otras cosas como estas)? IF RESPONDENT TRIED SEVERAL OF THESE DRUGS AT DIFFERENT AGES, ENTER THE EARLIEST AGE.	
	__	Answer must range from 2 to 12
	98	Refusal
	99	Don't know

Questions atod17 - atod26	
	Response Categories
	1 = Never/ Nunca
	2 = Less than once per week/ Menos que 1 vez por semana
	3= About once per week/ 1 vez por semana
	4 = Two to three times per week/ 2 o 3 veces por semana
	5 = (Almost) every- day/ (Casi) todos los días
	8 = Refusal
	9 = Don't know
atod17	In the past 3 months, how many times have you used or tried cigarettes? En los últimos tres meses, ¿cuántas veces has usado o probado cigarros?
atod18	In the past 3 months, how many times have you used or tried beer - more than just a few sips? En los últimos tres meses, ¿cuántas veces has usado o probado cerveza - más que unas pruebas?
atod19	In the past 3 months, how many times have you used or tried wine, or wine coolers - more than just a few sips? En los últimos tres meses, ¿cuántas veces has vino, o 'coolers' - más que unas pruebas?
atod20	In the past 3 months, how many times have you used or tried hard liquor? En los últimos tres meses, ¿cuántas veces has usado o probado licores fuertes?
atod21	In the past 3 months, how many times have you used or tried marijuana? En los últimos tres meses, ¿cuántas veces has usado o probado marihuana?
atod22	In the past 3 months, how many times have you used or tried inhalants? En los últimos tres meses, ¿cuántas veces has usado o probado inhalants?

atod23	In the past 3 months, how many times have you used or tried any other illegal drug? En los últimos tres meses, ¿cuántas veces has usado o probado otras drogas ilegales?	
atod24 (Asked of Child only)	In the past 3 months, how many times have you had four or more beers, glasses of wine or wine coolers, or shots of liquor in a row, within a few hours? En los últimos tres meses, ¿cuántas veces has tomado cuatro cervezas, vasos de vino, 'coolers' o tragos de licor en seguida, o dentro de unas cuantas horas?	
atod25 (Asked of Child only)	In the past 3 months, how many times have you had five or more beers, glasses of wine or wine coolers, or shots of liquor in a row, within a few hours? En los últimos tres meses, ¿cuántas veces has tomado cinco cervezas, vasos de vino, 'coolers' o tragos de licor en seguida, o dentro de unas cuantas horas?	
Atod26		
atod26 (Asked of Child only)	[Asked of Child only] On the days you drank alcohol during the past 3 months, how many beers, glasses of wine or wine cooler, or shots of liquor did you usually drink per day? Los días que tomaste alcohol durante los últimos tres meses, ¿cuántas cervezas, vasos de vino, 'coolers' o tragos de licor te tomabas normalmente en un solo día?	
	__	Answer must range from 1 to 15
	98	Refusal
	99	Don’t know

APPENDIX B

Supplementary Materials for Study 1

Table B1

Regression with Substance Use (Past 3 Months) Predicting Change in NAcc Response to Monetary Reward

Outcome	Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	Fit
Change in NAcc to Monetary Reward	(Intercept)	-0.04	[-0.10, 0.02]				
	Past 3 Months Use T1	-0.01	[-0.03, 0.01]	-0.10	[-0.26, 0.06]	.01	
	Gender	-0.03	[-0.11, 0.04]	-0.07	[-0.23, 0.09]	.01	
							R^2 = .014 95% CI [.00,.06]
	(Intercept)	-0.04	[-0.10, 0.02]				
	Past 3 Months Use T2	-0.01	[-0.02, 0.01]	-0.07	[-0.23, 0.10]	.00	
	Gender	-0.03	[-0.11, 0.05]	-0.06	[-0.23, 0.10]	.00	
							R^2 = .009 95% CI [.00,.05]
	(Intercept)	-0.07*	[-0.14, -0.01]				
	Past 3 Months Use T3	0.01	[-0.00, 0.02]	0.10	[-0.06, 0.27]	.01	
	Gender	-0.04	[-0.11, 0.04]	-0.08	[-0.24, 0.09]	.01	
							R^2 = .015 95% CI [.00,.07]
	(Intercept)	-0.05†	[-0.10, 0.00]				
	Change in Use T1-T2	0.00	[-0.01, 0.01]	0.02	[-0.15, 0.18]	.00	
	Gender	-0.03	[-0.11, 0.05]	-0.07	[-0.23, 0.09]	.00	
							R^2 = .005 95% CI [.00,.04]
	(Intercept)	-0.06*	[-0.12, -0.01]				
	Change in Use T2-T3	0.01	[-0.00, 0.02]	0.12	[-0.04, 0.29]	.02	
	Gender	-0.03	[-0.11, 0.04]	-0.07	[-0.23, 0.09]	.01	
							R^2 = .020 95% CI [.00,.08]
	(Intercept)	-0.07*	[-0.13, -0.01]				
	Change in Use T1-T3	0.01†	[-0.00, 0.02]	0.16	[-0.01, 0.32]	.02	
	Gender	-0.04	[-0.12, 0.04]	-0.08	[-0.25, 0.08]	.01	
							R^2 = .029 95% CI [.00,.09]

Note: N = 120. Corrected $^{+}p < 0.10$, $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, *b* = Unstandardized regression weights, *beta* = Standardized regression weights, sr^2 = Semi-partial correlation squared, CI = Confidence interval, *LL* and *UL* = Lower and upper limits of a confidence interval, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, and T3 = Time 3 when participants were approximately 21 years old. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Inclusion > Baseline in the Cyberball task. A significant *b*-weight indicates the beta-weight and semi-partial correlation are also significant. Change scores were arithmetic. Gender is coded as 0 = Women, 1 = Men.

Table B2

Regression with Substance Use (Past 3 Months) Predicting Change in mPFC Response to Monetary Reward

Outcome	Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	Fit
Change in mPFC to Monetary Reward	(Intercept)	0.05	[-0.00, 0.10]				
	Past 3 Months Use T1	-0.01	[-0.02, 0.01]	-0.08	[-0.25, 0.08]	.01	
	Gender	-0.03	[-0.10, 0.04]	-0.07	[-0.23, 0.09]	.01	
							R^2 = .012 95% CI [.00,.06]
	(Intercept)	0.05†	[0.00, 0.10]				
	Past 3 Months Use T2	-0.01	[-0.02, 0.01]	-0.10	[-0.26, 0.07]	.01	
	Gender	-0.03	[-0.09, 0.04]	-0.06	[-0.23, 0.10]	.00	
							R^2 = .014 95% CI [.00,.06]
	(Intercept)	0.05†	[-0.01, 0.10]				
	Past 3 Months Use T3	-0.00	[-0.01, 0.01]	-0.04	[-0.20, 0.13]	.00	
	Gender	-0.03	[-0.09, 0.04]	-0.07	[-0.23, 0.10]	.00	
							R^2 = .006 95% CI [.00,.04]
	(Intercept)	0.04†	[-0.01, 0.09]				
	Change in Use T1-T2	-0.00	[-0.01, 0.01]	-0.02	[-0.18, 0.15]	.00	
	Gender	-0.03	[-0.10, 0.04]	-0.07	[-0.23, 0.10]	.00	
							R^2 = .005 95% CI [.00,.04]
	(Intercept)	0.04	[-0.01, 0.09]				
	Change in Use T2-T3	0.00	[-0.01, 0.01]	0.02	[-0.14, 0.18]	.00	
	Gender	-0.03	[-0.10, 0.04]	-0.07	[-0.23, 0.09]	.00	
							R^2 = .005 95% CI [.00,.04]
	(Intercept)	0.04	[-0.01, 0.09]				
	Change in Use T1-T3	0.00	[-0.01, 0.01]	0.01	[-0.15, 0.17]	.00	
	Gender	-0.03	[-0.10, 0.04]	-0.07	[-0.23, 0.09]	.00	
							R^2 = .005 95% CI [.00,.04]

Note: N = 120. Corrected $^{\dagger}p < 0.10$, $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, *b* = Unstandardized regression weights, *beta* = Standardized regression weights, sr^2 = Semi-partial correlation squared, CI = Confidence interval, *LL* and *UL* = Lower and upper limits of a confidence interval, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, and T3 = Time 3 when participants were approximately 21 years old. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Inclusion > Baseline in the Cyberball task. A significant *b*-weight indicates the beta-weight and semi-partial correlation are also significant. Change scores were arithmetic. Gender is coded as 0 = Women, 1 = Men.

Table B3

Regression with Substance Use (Past 3 Months) Predicting Change in NAcc Response to Social Reward

Outcome	Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	Fit
Change in NAcc to Social Reward	(Intercept)	-0.01	[-0.08, 0.06]				
	Past 3 Months Use T1	-0.00	[-0.02, 0.02]	-0.03	[-0.20, 0.14]	.00	
	Gender	-0.06	[-0.15, 0.04]	-0.10	[-0.27, 0.07]	.01	
							R^2 = .011 95% CI [.00,.06]
	(Intercept)	0.01	[-0.06, 0.08]				
	Past 3 Months Use T2	-0.02†	[-0.04, 0.00]	-0.15	[-0.32, 0.01]	.02	
	Gender	-0.05	[-0.14, 0.05]	-0.08	[-0.25, 0.08]	.01	
							R^2 = .034 95% CI [.00,.10]
	(Intercept)	-0.03	[-0.11, 0.05]				
	Past 3 Months Use T3	0.00	[-0.01, 0.02]	0.05	[-0.12, 0.22]	.00	
	Gender	-0.06	[-0.15, 0.04]	-0.10	[-0.27, 0.07]	.01	
							R^2 = .013 95% CI [.00,.06]
	(Intercept)	-0.01	[-0.08, 0.05]				
	Change in Use T1-T2	-0.01	[-0.02, 0.01]	-0.09	[-0.26, 0.08]	.01	
	Gender	-0.06	[-0.15, 0.04]	-0.10	[-0.27, 0.07]	.01	
							R^2 = .018 95% CI [.00,.07]
	(Intercept)	-0.03	[-0.10, 0.04]				
	Change in Use T2-T3	0.01	[-0.00, 0.02]	0.13	[-0.04, 0.30]	.02	
	Gender	-0.06	[-0.15, 0.04]	-0.10	[-0.26, 0.07]	.01	
							R^2 = .027 95% CI [.00,.09]
	(Intercept)	-0.03	[-0.10, 0.05]				
	Change in Use T1-T3	0.00	[-0.01, 0.02]	0.06	[-0.10, 0.23]	.00	
	Gender	-0.06	[-0.15, 0.04]	-0.10	[-0.27, 0.07]	.01	
							R^2 = .014 95% CI [.00,.07]

Note: N = 120. Corrected $^{\dagger}p < 0.10$, $*p < 0.05$; $**p < 0.01$; $***p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, *b* = Unstandardized regression weights, *beta* = Standardized regression weights, sr^2 = Semi-partial correlation squared, CI = Confidence interval, *LL* and *UL* = Lower and upper limits of a confidence interval, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, and T3 = Time 3 when participants were approximately 21 years old. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Inclusion > Baseline in the Cyberball task. A significant *b*-weight indicates the beta-weight and semi-partial correlation are also significant. Change scores were arithmetic. Gender is coded as 0 = Women, 1 = Men.

Table B4

Regression with Substance Use (Past 3 Months) Predicting Change in mPFC Response to Social Reward

Outcome	Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	Fit
Change in mPFC to Social Reward	(Intercept)	0.12*	[0.02, 0.22]				
	Past 3 Months Use T1	-0.00	[-0.03, 0.03]	-0.01	[-0.18, 0.16]	.00	
	Gender	-0.04	[-0.18, 0.11]	-0.05	[-0.22, 0.12]	.00	
							R^2 = .002 95% CI [.00,.03]
	(Intercept)	0.12*	[0.01, 0.22]				
	Past 3 Months Use T2	0.00	[-0.03, 0.03]	0.01	[-0.16, 0.18]	.00	
	Gender	-0.04	[-0.18, 0.10]	-0.05	[-0.22, 0.12]	.00	
							R^2 = .002 95% CI [.00,.03]
	(Intercept)	0.11†	[-0.00, 0.23]				
	Past 3 Months Use T3	0.00	[-0.02, 0.02]	0.01	[-0.16, 0.18]	.00	
	Gender	-0.04	[-0.18, 0.10]	-0.05	[-0.22, 0.12]	.00	
							R^2 = .002 95% CI [.00,.03]
	(Intercept)	0.12*	[0.02, 0.22]				
	Change in Use T1-T2	0.00	[-0.02, 0.02]	0.01	[-0.16, 0.18]	.00	
	Gender	-0.04	[-0.18, 0.10]	-0.05	[-0.22, 0.12]	.00	
							R^2 = .002 95% CI [.00,.03]
	(Intercept)	0.12*	[0.01, 0.22]				
	Change in Use T2-T3	0.00	[-0.02, 0.02]	0.00	[-0.17, 0.17]	.00	
	Gender	-0.04	[-0.18, 0.10]	-0.05	[-0.22, 0.12]	.00	
							R^2 = .002 95% CI [.00,.03]
	(Intercept)	0.11*	[0.01, 0.22]				
	Change in Use T1-T3	0.00	[-0.02, 0.02]	0.01	[-0.16, 0.18]	.00	
	Gender	-0.04	[-0.18, 0.10]	-0.05	[-0.22, 0.12]	.00	
							R^2 = .002 95% CI [.00,.03]

Note: N = 120. Corrected $^{\dagger}p < 0.10$, $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, *b* = Unstandardized regression weights, *beta* = Standardized regression weights, sr^2 = Semi-partial correlation squared, CI = Confidence interval, *LL* and *UL* = Lower and upper limits of a confidence interval, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, and T3 = Time 3 when participants were approximately 21 years old. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Inclusion > Baseline in the Cyberball task. A significant *b*-weight indicates the beta-weight and semi-partial correlation are also significant. Change scores were arithmetic. Gender is coded as 0 = Women, 1 = Men.

Table B5

Regression with Substance Use (Past 2 Years) Predicting Change in NAcc Response to Monetary Reward

Outcome	Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	Fit
Change in NAcc to Monetary Reward	(Intercept)	-0.05	[-0.11, 0.02]				
	Past 2 Years Use T1	-0.00	[-0.02, 0.02]	-0.01	[-0.18, 0.15]	.00	
	Gender	-0.03	[-0.11, 0.05]	-0.07	[-0.23, 0.09]	.00	
							R^2 = .005 95% CI [.00,.04]
	(Intercept)	0.02	[-0.10, 0.05]				
	Past 2 Years Use T2	-0.01	[-0.04, 0.01]	-0.09	[-0.25, 0.07]	.01	
	Gender	-0.03	[-0.11, 0.04]	-0.07	[-0.23, 0.09]	.00	
							R^2 = .012 95% CI [.00,.06]
	(Intercept)	-0.05	[-0.13, 0.03]				
	Past 2 Years Use T3	-0.00	[-0.02, 0.02]	-0.00	[-0.17, 0.16]	.00	
	Gender	-0.03	[-0.11, 0.05]	-0.07	[-0.23, 0.10]	.00	
							R^2 = .005 95% CI [.00,.04]
	(Intercept)	-0.04	[-0.10, 0.02]				
	Change in Use T1-T2	-0.02	[-0.05, 0.01]	-0.10	[-0.26, 0.06]	.01	
	Gender	-0.03	[-0.11, 0.05]	-0.07	[-0.23, 0.10]	.00	
							R^2 = .015 95% CI [.00,.07]
	(Intercept)	-0.06*	[-0.12, -0.00]				
	Change in Use T2-T3	0.01	[-0.01, 0.03]	0.08	[-0.08, 0.24]	.01	
	Gender	-0.03	[-0.11, 0.05]	-0.07	[-0.23, 0.10]	.00	
							R^2 = .011 95% CI [.00,.06]
	(Intercept)	-0.05†	[-0.11, 0.01]				
	Change in Use T1-T3	0.00	[-0.02, 0.02]	0.01	[-0.15, 0.17]	.00	
	Gender	-0.03	[-0.11, 0.05]	-0.07	[-0.23, 0.10]	.00	
							R^2 = .005 95% CI [.00,.04]

Note: N = 120. Corrected $^{\dagger}p < 0.10$, $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, *b* = Unstandardized regression weights, *beta* = Standardized regression weights, sr^2 = Semi-partial correlation squared, CI = Confidence interval, *LL* and *UL* = Lower and upper limits of a confidence interval, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, and T3 = Time 3 when participants were approximately 21 years old. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Inclusion > Baseline in the Cyberball task. A significant *b*-weight indicates the beta-weight and semi-partial correlation are also significant. Change scores were arithmetic. Gender is coded as 0 = Women, 1 = Men.

Table B6

Regression with Substance Use (Past 2 Years) Predicting Change in mPFC Response to Monetary Reward

Outcome	Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	Fit
Change in mPFC to Monetary Reward	(Intercept)	0.05†	[-0.01, 0.10]				
	Past 2 Years Use T1	-0.01	[-0.02, 0.01]	-0.05	[-0.21, 0.12]	.00	
	Gender	-0.03	[-0.10, 0.04]	-0.07	[-0.23, 0.09]	.00	
							R^2 = .007 95% CI [.00,.04]
	(Intercept)	0.04	[-0.02, 0.10]				
	Past 2 Years Use T2	0.00	[-0.02, 0.02]	0.00	[-0.16, 0.17]	.00	
	Gender	-0.03	[-0.10, 0.04]	-0.07	[-0.23, 0.09]	.00	
							R^2 = .005 95% CI [.00,.04]
	(Intercept)	0.06	[-0.01, 0.12]				
	Past 2 Years Use T3	-0.01	[-0.02, 0.01]	-0.05	[-0.21, 0.12]	.00	
	Gender	-0.03	[-0.10, 0.04]	-0.07	[-0.23, 0.09]	.01	
							R^2 = .007 95% CI [.00,.05]
	(Intercept)	0.04	[-0.01, 0.08]				
	Change in Use T1-T2	0.01	[-0.02, 0.04]	0.07	[-0.09, 0.23]	.00	
	Gender	-0.03	[-0.10, 0.04]	-0.07	[-0.23, 0.09]	.00	
							R^2 = .009 95% CI [.00,.05]
	(Intercept)	0.05†	[-0.00, 0.09]				
	Change in Use T2-T3	-0.01	[-0.02, 0.01]	-0.05	[-0.21, 0.11]	.00	
	Gender	-0.03	[-0.10, 0.04]	-0.07	[-0.23, 0.09]	.01	
							R^2 = .007 95% CI [.00,.05]
	(Intercept)	0.04	[-0.01, 0.09]				
	Change in Use T1-T3	-0.00	[-0.02, 0.02]	-0.00	[-0.17, 0.16]	.00	
	Gender	-0.03	[-0.10, 0.04]	-0.07	[-0.23, 0.09]	.00	
							R^2 = .005 95% CI [.00,.04]

Note: N = 120. Corrected $^{\dagger}p < 0.10$, $*p < 0.05$; $**p < 0.01$; $***p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, *b* = Unstandardized regression weights, *beta* = Standardized regression weights, sr^2 = Semi-partial correlation squared, CI = Confidence interval, *LL* and *UL* = Lower and upper limits of a confidence interval, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, and T3 = Time 3 when participants were approximately 21 years old. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Inclusion > Baseline in the Cyberball task. A significant *b*-weight indicates the beta-weight and semi-partial correlation are also significant. Change scores were arithmetic. Gender is coded as 0 = Women, 1 = Men.

Table B7

Regression with Substance Use (Past 2 Years) Predicting Change in NAcc Response to Social Reward

Outcome	Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	Fit
Change in NAcc to Social Reward	(Intercept)	-0.03	[-0.11, 0.05]				
	Past 2 Years Use T1	0.01	[-0.02, 0.04]	0.08	[-0.09, 0.25]	.01	
	Gender	-0.06	[-0.16, 0.04]	-0.10	[-0.27, 0.06]	.01	
							R^2 = .016 95% CI [.00,.07]
	(Intercept)	-0.03	[-0.11, 0.06]				
	Past 2 Years Use T2	0.01	[-0.02, 0.03]	0.03	[-0.14, 0.20]	.00	
	Gender	-0.06	[-0.16, 0.04]	-0.10	[-0.27, 0.07]	.01	
							R^2 = .011 95% CI [.00,.06]
	(Intercept)	-0.04	[-0.14, 0.06]				
	Past 2 Years Use T3	0.01	[-0.02, 0.03]	0.05	[-0.12, 0.22]	.00	
	Gender	-0.05	[-0.15, 0.04]	-0.09	[-0.26, 0.08]	.01	
							R^2 = .013 95% CI [.00,.06]
	(Intercept)	-0.01	[-0.08, 0.06]				
	Change in Use T1-T2	-0.01	[-0.05, 0.03]	-0.06	[-0.23, 0.11]	.00	
	Gender	-0.06	[-0.15, 0.04]	-0.10	[-0.27, 0.07]	.01	
							R^2 = .014 95% CI [.00,.06]
	(Intercept)	-0.02	[-0.09, 0.05]				
	Change in Use T2-T3	0.00	[-0.02, 0.03]	0.02	[-0.15, 0.19]	.00	
	Gender	-0.05	[-0.15, 0.04]	-0.10	[-0.27, 0.08]	.01	
							R^2 = .010 95% CI [.00,.06]
	(Intercept)	-0.01	[-0.09, 0.06]				
	Change in Use T1-T3	-0.00	[-0.03, 0.02]	-0.02	[-0.19, 0.15]	.00	
	Gender	-0.06	[-0.16, 0.04]	-0.10	[-0.27, 0.07]	.01	
							R^2 = .010 95% CI [.00,.06]

Note: N = 120. Corrected $^{\dagger}p < 0.10$, $*p < 0.05$; $**p < 0.01$; $***p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, *b* = Unstandardized regression weights, *beta* = Standardized regression weights, sr^2 = Semi-partial correlation squared, CI = Confidence interval, *LL* and *UL* = Lower and upper limits of a confidence interval, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, and T3 = Time 3 when participants were approximately 21 years old. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Inclusion > Baseline in the Cyberball task. A significant *b*-weight indicates the beta-weight and semi-partial correlation are also significant. Change scores were arithmetic. Gender is coded as 0 = Women, 1 = Men.

Table B8

Regression with Substance Use (Past 2 Years) Predicting Change in mPFC Response to Social Reward

Outcome	Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	Fit
Change in mPFC to Social Reward	(Intercept)	0.11†	[-0.01, 0.22]				
	Past 2 Years Use T1	0.01	[-0.03, 0.05]	0.03	[-0.14, 0.20]	.00	
	Gender	-0.04	[-0.19, 0.10]	-0.05	[-0.22, 0.12]	.00	
							R^2 = .003 95% CI [.00,.03]
	(Intercept)	0.12†	[-0.01, 0.24]				
	Past 2 Years Use T2	0.00	[-0.04, 0.04]	0.00	[-0.17, 0.17]	.00	
	Gender	-0.04	[-0.18, 0.10]	-0.05	[-0.22, 0.12]	.00	
							R^2 = .002 95% CI [.00,.03]
	(Intercept)	0.09	[-0.06, 0.23]				
	Past 2 Years Use T3	0.01	[-0.03, 0.05]	0.05	[-0.12, 0.22]	.00	
	Gender	-0.03	[-0.18, 0.11]	-0.04	[-0.21, 0.13]	.00	
							R^2 = .004 95% CI [.00,.04]
	(Intercept)	0.12*	[0.02, 0.23]				
	Change in Use T1-T2	-0.01	[-0.07, 0.04]	-0.04	[-0.21, 0.13]	.00	
	Gender	-0.04	[-0.18, 0.11]	-0.05	[-0.22, 0.12]	.00	
							R^2 = .004 95% CI [.00,.03]
	(Intercept)	0.11*	[0.00, 0.21]				
	Change in Use T2-T3	0.01	[-0.03, 0.05]	0.04	[-0.13, 0.22]	.00	
	Gender	-0.03	[-0.18, 0.11]	-0.04	[-0.21, 0.13]	.00	
							R^2 = .004 95% CI [.00,.04]
	(Intercept)	0.11*	[0.00, 0.22]				
	Change in Use T1-T3	0.00	[-0.03, 0.04]	0.02	[-0.15, 0.19]	.00	
	Gender	-0.04	[-0.18, 0.11]	-0.04	[-0.22, 0.13]	.00	
							R^2 = .002 95% CI [.00,.03]

Note: N = 120. Corrected $^{+}p < 0.10$, $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$. NAcc = Nucleus accumbens, mPFC = Medial prefrontal cortex, *b* = Unstandardized regression weights, *beta* = Standardized regression weights, sr^2 = Semi-partial correlation squared, CI = Confidence interval, *LL* and *UL* = Lower and upper limits of a confidence interval, T1 = Time 1 when participants were approximately 17 years old, T2 = Time 2 when participants were approximately 19 years old, and T3 = Time 3 when participants were approximately 21 years old. Monetary Reward represents neural response in the contrast Gain Anticipation > Neutral Anticipation in the Monetary Incentive Delay task, and Social Reward represents neural response in the contrast Inclusion > Baseline in the Cyberball task. A significant *b*-weight indicates the beta-weight and semi-partial correlation are also significant. Change scores were arithmetic. Gender is coded as 0 = Women, 1 = Men.

APPENDIX C

Supplementary Materials for Study 2

Supplement C1

Questionnaire Used to Assess Social Support

Multidimensional Scale of Perceived Social Support (MSPSS, 13 items)

DESCRIPTION

Originally developed in the late 1980s, this measure was intended to require only a minimal reading level, to be short, and to assess support from multiple classes of supporters (Zimet, Dahlem, Zimet, & Farley, 1988). It assesses perceived social support from family and friends. The original scale included a measure for social support from a "significant other", but this does not seem appropriate for adolescents. Each subscale in the original version had an alpha coefficient of at least .89 and the overall reliability was .93 (Canty-Mitchell & Zimet, 2000). Items were changed from a five-point scale to a four-point scale.

ASSOCIATED PAPERS

Canty-Mitchell, J., & Zimet, G.D. (2000). Psychometric properties of the Multidimensional Scale of Perceived Social Support in urban adolescents. *American Journal of Community Psychology, 28,* 391-400.

Zimet, G.D., Dahlem, N.W., Zimet, S.G., & Farley, G.K. (1988). The Multidimensional Scale of Perceived Social Support. *Journal of Personality Assessment, 52,* 30-41.

Now please think about all the family members who live with you such as your parent(s) (and any brothers or sisters), and please tell me how true each of these statements is. **Ahora piensa por favor en tu familia más cercana, tu mamá, (si se aplica, tu papá), (y si se aplica, tus hermanos); por favor dime que tan cierta es cada una de estas frases.**	
Response Categories:	
1 = Not at all true/ Nada cierto	
2= Somewhat true/ Algo cierto	
3= Mostly true/ Cierto	
4= Very true/ Muy cierto	
8= Refusal	
9= Don't know	
msps01	Your family really tries to help you. Tu familia de verdad trata de ayudarte.
msps02	When you feel bad, you get the help and support you need from your family. Cuando te sientes mal, recibes la ayuda y el apoyo que necesitas de tu familia.
msps03	You can talk about your problems with your family. Puedes hablar de tus problemas con tu familia.

msps04	Your family is willing to help you make decisions. Tu familia está dispuesta ayudarte a tomar decisiones.	
Now think about your friends and tell me how true each of these statements is. Ahora piensa en tus amigos y dime qué tan cierta es cada una de estas frases.		
msps05	Your friends really try to help you. Tus amigos de verdad tratan de ayudarte.	
msps06	You can count on your friends when things go wrong. Puedes contar con tus amigos cuando las cosas no van bien.	
msps07	You have friends with whom you can share your joys and sorrows. Tienes amigos con quienes puedes compartir tus alegrías y tus tristezas.	
msps08	You can talk about your problems with your friends. Puedes hablar sobre tus problemas con tus amigos.	
Now I would like to ask you some questions about your relation with some important people in your life. Ahora me gustaría preguntarte unas preguntas acerca de tus relaciones con algunas personas importantes en tu vida.		
msps13	Do you have anyone with whom you can share your innermost thoughts and feelings? Please just answer Yes or No. ¿Tienes alguna persona con quien puedes compartir tus pensamientos o sentimientos más íntimos? Por favor solamente contesta Sí o No.	
	1	Yes/Sí
	2	No/No
	3	Not applicable (Not asked at Wave 1 for Mom and Dad, or for Child)
	8	Refusal
	9	Don’t know

Supplement C2

Questionnaire Used to Assess Familism

Mexican-American Acculturation/Enculturation Scale (MACVS, 50 items)

DESCRIPTION

The Mexican American Acculturation/Enculturation Scale - Values was developed by Knight et al. (2010). Their purpose was to develop a measure of acculturation and enculturation for Mexican Americans that is broader than, and addresses the limitations of, the currently available measures. The scale was developed based upon focus groups conducted with Mexican American mothers, fathers, and adolescents about the Mexican American and Anglo American cultures. Some of the items are minor re-wording of specific parent or adolescent statements made during the focus groups. Some of the items were created to reflect general topic of discussion by the focus groups. Some of the items were adapted from other measures of similar constructs. Items 6, 16, 17, 27, 29, & 49 were taken from Sabogal et al. (1987).

This scale is designed to be applicable to either parent or adolescent respondents. An earlier version of the scale contained 63 items that assessed 11 subscales of values that are likely to change through the processes of acculturation and enculturation. Based on confirmatory factor analysis, 13 items were found not to fit into the measurement models for their respective subscales or their subscales were found to have very poor psychometric properties (i.e., egalitarian gender roles and personal freedom). These findings were replicated. As a result, this study dropped those 13 items and only used 50 items which assess 9 subscales of values.

ASSOCIATED PAPERS

Knight, G.P., Gonzales, N.A., Saenz, D.S., Bonds, D.D., Germán, M., Deardorff, J., Roosa, M.W., & Updegraff, K.A. (2010). The Mexican American cultural values scales for adolescents and adults. *Journal of Early Adolescence*, *30*, 444-481.

Please tell me how much you agree with the following statements. Por favor dime ¿cuánto estás de acuerdo o desacuerdo con las siguientes frases?	
Response Categories	
1 = Not at all/ Nada	
2 = A little/ Un poco	
3= Somewhat/ Algo	
4 = Very much/ Bastante	
8 = Refusal	
9 = Don't know	
macvs01	How much do you agree that parents should teach their children to pray? ¿Qué tan de acuerdo estás que los padres deberían enseñarle a sus hijos a rezar?
macvs02	How much do you agree that parents should teach their children that the family always comes first? ¿Qué tan de acuerdo estás que los padres deberían enseñarle a sus hijos que la familia siempre es primero?
macvs03	Children should be taught that it is their duty to care for their parents when their parents get old.

	Se les debería enseñar a los niños que es su obligación cuidar a sus padres cuando ellos se hagan viejos.
macvs04	Children should always do things to make their parents happy. Los niños siempre deberían hacer las cosas que hagan a sus padres felices.
macvs05	How much do you agree that, no matter what, children should always treat their parents with respect? ¿Qué tan de acuerdo estás que sea lo que sea, los niños siempre deberían tratar a sus padres con respeto?
macvs06	Children should be taught that it is important to have a lot of money. Se les debería enseñar a los niños que es importante tener mucho dinero.
macvs07	People should learn how to take care of themselves and not depend on others. La gente debería aprender cómo cuidarse ellos mismos y no contar con otra gente.
macvs08	God is first; family is second. Dios está primero, la familia está en segundo lugar.
macvs09	Family provides a sense of security because they will always be there for you. La familia provee un sentido de seguridad, porque ellos siempre estarán alli para ti.
macvs10	How much do you agree that children should respect adult relatives as if they were parents? ¿Qué tan de acuerdo estás que los niños deberían respetar a parientes mayores como si fueran sus padres?
macvs11	If a relative is having a hard time financially, one should help him or her out if possible. Si un pariente tiene dificultades económicas, uno debería ayudarle si puede.
macvs12	When it comes to important decisions, the family should ask for advice from close relatives. Cuando se trata de decisiones importantes, la familia debería pedir consejos a los parientes mas cercanos.
macvs13	Men should earn most of the money for the family so women can stay home and take care of the children and the home. Los hombres deberían ganar la mayoría del dinero en la familia para que las mujeres puedan quedarse en casa y cuidar a los hijos y el hogar.
macvs14	One must be ready to compete with others to get ahead. Uno tiene que estar listo para competir con otros si uno quiere salir adelante.
macvs15	Children should never question their parents' decisions. Los hijos nunca deberían cuestionar las decisiones de sus padres.
macvs16	Money is the key to happiness. El dinero es la clave para la felicidad.
macvs17	The most important thing parents can teach their children is to be independent from others. Lo más importante que los padres pueden enseñarle a sus hijos es que sean independientes de otros.
macvs18	One's belief in God gives inner strength and meaning to life. La creencia en Dios da fuerza interna y significado a la vida.
macvs19	Families need to watch over and protect teenage girls more than teenage boys. Las familias necesitan vigilar y proteger más a las niñas adolescentes que a los niños adolescentes.

macvs20	It is always important to be united as a family. Siempre es importante estar unidos como familia.
macvs21	How much do you believe that a person should share his or her home with relatives if they need a place to stay? ¿Qué tan de acuerdo estás que uno debería de compartir su casa con parientes si ellos necesitan un lugar donde quedarse?
macvs22	Children should be on their best behavior when visiting the homes of friends or relatives. Los niños deberían portarse de la mejor manera cuando visitan las casas de amigos o familiares.
macvs23	Parents should encourage children to do everything better than others. Los padres deberían animar a los hijos para que hagan todo mejor que los demás.
macvs24	Owning a lot of nice things makes one very happy. Tener muchas cosas buenas lo hace a uno muy felíz.
macvs25	Children should always honor their parents and never say bad things about them. Los niños siempre deberían honrar a sus padres y nunca decir cosas malas de ellos.
macvs26	As children get older their parents should allow them to make their own decisions. Según los niños van creciendo, los padres deberían dejar que ellos tomen sus propias decisiones.
macvs27	If everything is taken away, one still has his or her faith in God. Si a uno le quitan todo, todavía le queda la fe en Dios.
macvs28	It is important to have close relationships with aunts, uncles, grandparents and cousins. Es importante mantener relaciones cercanas con tíos, abuelos y primos.
macvs29	Older kids should take care of and be role models for their younger brothers and sisters. Los hermanos mayores deberían cuidar y darles el buen ejemplo a los hermanos menores.
macvs30	How much do you agree that children should be taught to always be good because they represent the family? ¿Qué tan de acuerdo estás que se les debe enseñar a los niños a que siempre sean buenos porque ellos representan a la familia?
macvs31	Children should follow their parents' rules, even if they think the rules are unfair. Los niños deberían seguir las reglas de sus padres, aún cuando piensen que no son justas.
macvs32	It is important for the man to have more power in the family than the woman. En la familia es importante que el hombre tenga más poder que la mujer.
macvs33	Personal achievements are the most important things in life. Los logros personales son las cosas más importantes en la vida.
macvs34	The more money one has, the more respect he or she should get from others. Entre más dinero tenga uno, más respeto debería recibir.
macvs35	When there are problems in life, a person can only count on himself or herself. Cuando hay problemas en la vida, uno sólo puede contar con sí mismo.
macvs36	It is important to thank God everyday for all one has. Es importante darle gracias a Dios todos los días por todo lo que uno tiene.
macvs37	Holidays and celebrations are important because the whole family comes together.

	Los días festivos y las celebraciones son importantes porque se reúne toda la familia.
macvs38	Parents should be willing to make great sacrifices to make sure their children have a better life. Los padres deberían estar dispuestos hacer grandes sacrificios para asegurarse que sus hijos tengan una vida mejor.
macvs39	A person should always think about his/her family when making important decisions. Uno siempre debería considerar a su familia cuando toma decisiones importantes.
macvs40	It is important for children to understand that their parents should have the final say when decisions are made in the family. Es importante que los niños entiendan que sus padres deberían tener la última palabra cuando se toman decisiones en la familia.
macvs41	How much do you agree that parents should teach their children to compete to win? ¿Qué tan de acuerdo estás que los padres deberían enseñarle a sus hijos a competir para ganar?
macvs42	Mothers are the main person responsible for raising children. Las madres son las personas principales responsables por la crianza de los hijos.
macvs43	The best way for a person to feel good about himself or herself is to have a lot of money. La mejor manera de sentirse bien acerca de uno mismo es tener mucho dinero.
macvs44	Parents should encourage children to solve their own problems. Los padres deberían animar a sus hijos a que resuelvan sus propios problemas.
macvs45	It is important to follow the Word of God. Es importante seguir la palabra de Dios.
macvs46	It is important for family members to show their love and affection to one another. Es importante que los miembros de la familia muestren su amor y afecto unos a los otros.
macvs47	It is important to work hard and do one s best because this work reflects on the family. Es importante trabajar duro y hacer lo mejor que uno pueda porque el trabajo de uno se refleja en la familia.
macvs48	Religion should be an important part of one's life. La religión debería ser una parte importante de la vida de uno.
macvs49	Children should always be polite when speaking to any adult. Los niños siempre deberían ser amables cuando hablan con cualquier adulto.
macvs50	How much do you agree that a wife should always support her husbands' decisions, even if she does not agree with him? ¿Qué tan de acuerdo estás que la esposa siempre debería apoyar las decisiones de su esposo, aunque no esté de acuerdo con él?

Note: Familism was calculated with items 2, 3, 4, 9, 11, 12, 20, 21, 28, 29, 30, 37, 38, 39, 46, and 47 (16 items total).

Supplement C3

Questionnaire Used to Assess Peer Victimization

Relational Aggression Scale: Victim (RAGV, 12 items)

DESCRIPTION

The Relational Aggression Scale was adapted from Prinstein et al.'s (2001) version of the Revised Peer Experiences Questionnaire (Vernberg et al, 1999), which assesses adolescents' aggression and victimization experiences (items 1 – 5), Neary & Joseph's (1994) Peer Victimization Scale (items 6-8), Nadeem and Graham's Self-Perceived Victimization scale (items 9 -11), and one item from Kokkinos and Panayiotou's Bullying and Victimisation Questionnaire (2004) (item 12). Relational aggression, in contrast to overt aggression, denotes non-physical behaviors that are intended to inflict social harm on victims (Crick, 1995, 1997) and has been linked to psychological distress in school-age children, namely depression (Crick & Bigbee, 1998).

The items in this subscale were adapted by the La Familia team for younger children (i.e., using the phrase "a kid your age" instead of "a teen" to refer to the aggressor). Additionally, the original scale is written in the 1st person; it was rewritten in the 2nd person to be more consistent with the La Familia battery. The response categories were modified from the original 5-point Likert-type scale to a 4-point Likert-type scale, and the response options were reversed so that a higher score reflects higher levels of aggression as set forth below.

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Crick, N. R., & Bigbee, M. A. (1998). Relational and overt forms of peer victimization: A multiinformant approach. *Journal of Consulting and Clinical Psychology, 66,* 337-347.

Kokkinos, C.M., & Panayiotou, G. (2004). Predicting bullying and victimization among early adolescents: Associations with disruptive behavior disorders. *Aggressive Behavior, 30,* 520-533.

Neary, A., & Joseph, S. (1994). Peer victimization and its relationship to self-concept and depression among schoolgirls. Personality and Individual Differences, 15, 183-186.

Prinstein, M.J., Boergers, J., & Vernberg, E.M. (2001). Overt and relational aggression in adolescents: Social-psychological adjustment of aggressors and victims. *Journal of Clinical Child Psychology, 30,* 479-491.

Vernberg, E.M., Jacobs, A.K., & Hershberger, S.L. (1999). Peer victimization and attitudes about violence during early adolescence. *Journal of Clinical Child Psychology, 28,* 386-395.

Please tell me how often you did each of the following things in the past 3 months.
Por favor, dime cuántas veces tú hiciste las siguientes cosas en los últimos 3 meses.

	Response Categories:
	1 = Almost never or never/ Casi nunca o nunca
	2= Sometimes/ A veces
	3= A lot of the time/ Muchas veces
	4= Almost always or always/ Casi siempre o siempre
	8= Refusal
	9= Don't know
ragv01	In the past 3 months, a kid your age left you out of what he or she was doing. En los últimos tres meses, otro niño de tu edad te dejó fuera de lo que él o ella estaba hacienda.
ragv02	In the past 3 months, a kid your age left you out of an activity or conversation that you really wanted to be included in. En los últimos tres meses, otro niño de tu edad te dejó fuera de una actividado conversación en la que tú ealmente queries ser incluido/a.
ragv03	In the past 3 months, a kid your age did not invite you to a party or other social event even though he or she knew that you wanted to go. En los últimos tres meses, otro niño de tu edad no te invitó a una fiesta u otro evento social, aún cuando él o ella sabía que querías ir.
ragv04	A kid your age that you like would not sit near you at lunch or in class. Otro niño de tu edad con quien quieres ser amigo no quiso sentarse cerca de ti durante el almuerzo o en clase.
ragv05	A kid your age gave you the silent treatment or did not talk to you on purpose. Otro niño de tu edad ya no te quizo hablar.
ragv06	A kid your age picked on you. Otro niño de tu edad estaba molestándote.
ragv07	A kid your age pushed you around or hit you. Otro niño de tu edad te empujó o te pegó.
ragv08	A kid your age said mean or bad things to you. Otro niño de tu edad te dijo cosas feas o cosas malas.
ragv09	A kid your age told mean stories or lies about you. Otro niño de tu edad estuvo contando cosas malas o mentiras de ti.
ragv10	A kid your age stole things from you. Otro niño de tu edad se robó cosas tuyas.
ragv11	A kid your age broke or destroyed your things. Otro niño de tu edad quebró o distruyó cosas tuyas.
ragv12	A kid your age made fun of the way you look. Otro niño de tu edad se burló de tu apariencia.

Supplement C4

Questionnaire Used to Assess Ethnic-Racial Discrimination

Adolescent Perceptions of Discrimination (DSCR, 19 items)

DESCRIPTION

This scale assesses adolescents' perceptions of discrimination against their racial/ethnic group in general as well as their experiences with prejudice and discrimination directed at them. Kristen Johnston and Melissa Delgado (2004) based the questions on Hughes and Dodge's (1997) Racism in the Workplace Scale and Klonoff and Landrine's (1995) Schedule of Sexist Events. The measure has two subscales: Perceptions of General Racism, and Personal Experiences with Prejudice and Discrimination. Each subscale has four domains: Teachers, Peers at school, Neighborhood, and Strangers. For this study, the target ethnic group in each question was intended to be the ethnic group with which the respondent most identifies. The first ten items are from the La Familia project, the remaining eight items were created based on another scale labeled "Perceptions of racial/ethnic bias against Mexican-origin students" provided by Manuel Barajas (professor at California State University, Sacramento).

ASSOCIATED PAPERS

Hughes, D., & Dodge, M. A. (1997). African American women in the workplace: Relationships between job conditions, racial bias at work, and perceived job quality. *American Journal of Community Psychology, 25*, 581-599.

Johnston, K.E. & Delgado, M.Y. (2004). Mexican American adolescents' experiences with ethnic discrimination. Poster presentation at the Biennial Conference of the Society for Research on Adolescence, Baltimore, Maryland.

Klonoff, E.A., & Landrine, H. (1995). The schedule of sexist events: A measure of lifetime and recent sexist discrimination in women's lives. *Psychology of Women Quarterly, 19*, 439-472.

Landrine, H., Klonoof, E.A., Gibbs, J., Manning, V., & Lund, M. (1995). Physical and psychiatric correlates of gender discrimination. *Psychology of Women Quarterly, 19*, 473-492.

For the next set of questions, I am interested in your experiences with other people, in your neighborhood and at school. Tell me how true the following statements are for you. **Para las siguientes preguntas estoy interesado/a en tus experiencias con otras personas, en tu vecindad y en tu escuela. Dime que tan ciertas son para ti las siguientes frases.**
Response Categories:
1 = Not at all true/ Nada cierto
2= Somewhat true/ Algo cierto
3= Mostly true/ Cierto
4= Very true/ Muy cierto
8= Refusal
9= Don't know

dscr01	Your teachers think all [Mexicans/Mexican-Americans] are alike. Tus maestros piensan que todos los [Mexicanos/México-Americanos] son iguales.
dscr02	You have heard kids at school making jokes or saying bad things about [Mexicans/Mexican-Americans]. Has oído a niños en tu escuela haciendo bromas o diciendo cosas malas de los [Mexicanos/México-Americanos].
dscr03	Kids at school think bad things about [Mexicans/Mexican-Americans]. Niños en la escuela piensan mal sobre los [Mexicanos/México-Americanos].
dscr04	Your teachers dislike [Mexicans/Mexican-Americans]. A tus maestros no les gustan los [Mexicanos/México-Americanos].
dscr05	Kids at school dislike [Mexicans/Mexican-Americans]. A los niños de la escuela no les gustan los [Mexicanos/México-Americanos].
dscr06	You have heard your teachers at school making jokes or saying bad things about [Mexicans/Mexican-Americans]. Has oído a tus maestros en tu escuela haciendo bromas o diciendo cosas malas de los [Mexicanos/México-Americanos].

Thinking about these people, please tell me how often each of the following things happened to you in the past 3 months. **Pensando en estas personas dime, en los últimos 3 meses, que tan seguido te ha sucedido cada una de las siguientes cosas.**	
	Response Categories:
	1 = Almost never or never/ Casi nunca o nunca
	2= Sometimes/ A veces
	3= A lot of the time/ Muchas veces
	4= Almost always or always/ Casi siempre o siempre
	8= Refusal
	9= Don't know
dscr07	How often have kids at school excluded you from their activities, like not inviting you to go out with them, not inviting you to their houses, or not letting you join their games, because you are [Mexican/Mexican-American]? ¿Qué tan seguido los niños de tu escuela te excluyeron de sus actividades, así como: invitarte a salir con ellos, o a sus casas, o jugar con ellos porque eres [Mexicano/México-Americano]?
dscr08	How often have you had to work harder in school than White kids to get the same praise or the same grades from your teachers because you are [Mexican/Mexican-American]? ¿Qué tan seguido tuviste que trabajar más que los niños anglosajones en la escuela para que tu maestro/a te dijera cosas buenas o para recibir las mismas calificaciones, porque eres [Mexicano/México-Americano]?

dscr09	Have kids at school called you names because you are [Mexican/Mexican-American]? ¿Los niños de la escuela te dijeron malas palabras, porque eres [Mexicano/México-Americano]?
dscr10	Have your teachers expected you to misbehave more than other kids because you are [Mexican/Mexican-American]? ¿Tus maestros esperaban que te ibas a portar más mal que otros niños, o te castigaron más duro porque eres [Mexicano/México-Americano]?

Tell me how true the following statements are for you. **Dime que tan ciertas son para ti las siguientes frases.**	
Response Categories:	
1 = Not at all true/ Nada cierto	
2= Somewhat true/ Algo cierto	
3= Mostly true/ Cierto	
4= Very true/ Muy cierto	
8= Refusal	
9= Don't know	
dscr11	If you get bad grades, it is blamed on your family not valuing education Por tus malas calificaciones le echan la culpa a tu familia de no valorar la educación.
dscr12	You are taught about your Mexican heritage and history in the U.S. Aquí en los Estados Unidos, te enseñan acerca de tu herencia Mexicana e hístoria de México.
dscr13	Teachers think kids who speak Spanish don't do as well at school. Porque hablas español, se piensa que te límita en llegar a logros altos académicos.
dscr14	You are praised by your teacher because you do not speak English with a [Mexican/Mexican-American] accent. Te felicita tu maestro/a porque hablas ingles sin acento.
dscr15	The teacher has the same educational expectations for [Mexican/Mexican-American] children as for other children. Los maestros tienen las mismas esperanzas para la educación de estudiantes Mexicanos que tienen para otros estudiantes.
dscr16	[Mexican/Mexican-American] children are often placed in separate classrooms. A los estudiantes Mexicanos seguido los ponen en diferentes salones.
dscr17	Your classroom rules - for example about going to the restroom, coming in late, accepting late homework, and so on - are applied equally to all children regardless of race. Las reglas del salon - como cuando pueden ir al baño, que pasa si uno llega tarde, si se acepta la tarea tarde, y otras cosas - son las mismas para todos los alumnos sin fijarse en su raza.

Thinking about these people, please tell me how often each of the following things happened to you in the past 3 months. **Pensando en estas personas dime, en los últimos 3 meses, que tan seguido te ha sucedido cada una de las siguientes cosas.**	
	Response Categories:
	1 = Almost never or never/ Casi nunca o nunca
	2= Sometimes/ A veces
	3= A lot of the time/ Muchas veces
	4= Almost always or always/ Casi siempre o siempre
	8= Refusal
	9= Don't know
dscr18	Did people assume you are from another country because of your skin color? La gente piensa que eres de otro país por el color de tu piel.
dscr19	Have your teachers punished you more harshly because you are [Mexican/Mexican-American]? ¿Tus maestros te han castigado más duro porque eres Mexicano/México-Americano?

Note: Ethnic-racial discrimination was calculated with items 2, 3, 5, 7, and 9 (5 items total).

Supplement C5

Questionnaire Used to Assess Relationship Quality

Quality of Relationship (QRLI, 6 items)

DESCRIPTION

This scale was developed by Rand Conger from diverse sources. It is intended to serve as an overall evaluative judgment of the relationship.

ASSOCIATED PAPERS

Yeh, H-C, Lorenz, F. O., Wickrama, K. A. S., Conger, R. D., & Elder, G. H. (2006). Relationships among sexual satisfaction, marital quality, and marital instability at midlife. *Journal of Family Psychology, 20,* 339 - 343.

We are going to talk about [NAME] for a while. Please tell me how true each of the following statement is about your relationship with [NAME]. **Vamos hablar sobre [NAME] por un rato. Dígame que tan cierta es cada frase acerca de su relación con [NAME].**	
	Response Categories:
	1 = Not at all true/ Nada cierto
	2= Somewhat true/ Algo cierto
	3= Mostly true/ Cierto
	4= Very true/ Muy cierto
	8= Refusal
	9= Don't know
qrli01	You have a good relationship. Ustedes tienen una buena relación
qrli02	Your relationship with [FATHER] is very stable. Su relación con [FATHER] es muy estable.
qrli03	Your relationship is strong. Su relación es sólida.
qrli04	Your relationship with [FATHER] makes you happy. Su relación con [FATHER] la hace felíz.

qrli05	Everything considered, how happy are you in your relationship?	
	1	Very unhappy
	2	Fairly unhappy
	3	Fairly happy
	4	Very happy
	8	Refusal
	9	Don't know
qrli06	Everything considered, how satisfied are you in your relationship?	

	Tomando todo en cuenta, ¿qué tan satisfecho/a está usted en su relación?	
	1	Very unsatisfied/Muy insatisfecho/a
	2	Fairly unsatisfied /Más o menos insatisfecho/a
	3	Fairly satisfied /Algo satisfecho/a
	4	Very satisfied /Muy satisfecho/a
	8	Refusal
	9	Don’t know

Supplement C6

Questionnaire Used to Assess Resistance to Peer Influence

RPI (Resistance to Peer Influence)

Purpose: Measures an individual's resistance to peer influence
Reporter: Adolescent self-report
No. of items: 10
Data collection: Time 1
Variables: C03RPI01 – C03RPI10
Coding: 1 or 4 = Really True for me, 2 or 3 = Sort of True for me
Scoring: Score each item 1 to 4 (left to right). Reverse score, sum, and divide by number of responses.
Scoring notes: Reverse score 2, 6, and 10. A valid score can be obtained only if there are at least 7 responses.
Source: Steinberg, L., & Monahan, K. C. (2007). Age differences in resistance to peer influence. *Developmental Psychology, 43*(6), 1531-1543. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2779518/table/T6/

RPI

Instructions
For each question, decide which sort of person you are most like — the one described on the right or the one described on the left. Then decide if that is "sort of true" or "really true" for you, and mark that choice. **For each line mark only ONE of the four choices.**

	Really True for Me	Sort of True for Me				Sort of True for Me	Really True for Me
1.	❑	❑	Some people go along with their friends just to keep their friends happy	**BUT**	Other people refuse to go along with what their friends want to do, even though they know it will make their friends unhappy	❑	❑
2.	❑	❑	Some people think it is more important to be an individual than to fit in with the crowd	**BUT**	Other people think it is more important to fit in with the crowd than to stand out as an individual	❑	❑
3.	❑	❑	For some people it's pretty easy for their friends to get them to change their mind	**BUT**	For other people it's pretty hard for their friends to get them to change their mind	❑	❑

4.	❑	❑	Some people would do something that they knew was wrong just to stay on their friends' good side	**BUT**	Other people would not do something that they knew was wrong just to stay on their friends' good side	❑	❑
5.	❑	❑	Some people hide their true opinion from their friends if they think their friends will make fun of them because of it	**BUT**	Other people will say their true opinion in front of their friends even if they know their friends will make fun of them because of it	❑	❑
6.	❑	❑	Some people will not break the law just because their friends say that they would	**BUT**	Other people would break the law if their friends said that they would break it	❑	❑
7.	❑	❑	Some people change the way they act so much when they are with their friends that they wonder who they "really are"	**BUT**	Other people act the same way when they are alone as they do when they are with their friends	❑	❑
8.	❑	❑	Some people take more risks when they are with their friends than they do when they are alone	**BUT**	Other people act just as risky when they are alone as when they are with their friends	❑	❑
9.	❑	❑	Some people say things they don't really believe just because they think it will make their friends respect them more	**BUT**	Other people would not say things they didn't really believe just to get their friends to respect them more	❑	❑
10.	❑	❑	Some people think it is better to be an individual even if	**BUT**	Other people think it's better to go along with the	❑	❑

people will be angry at you for going against the crowd	crowd than to make people angry at you

Supplement C7

Questionnaire Used to Assess Prosocial Behavior

SDQ (Strengths and Difficulties Questionnaire)

Purpose: Assess social, emotional, and conduct strengths and difficulties
Reporter: Adolescent self-report
No. of items: 25
Data collection: Time 1
Variables: `C03SDQ01 – C03SDQ25; T2_C03SDQ01 – T2_C03SDQ25`
Coding: 0 = Not True, 1 = Somewhat True, 2 = Certainly True
Scoring: Sum items.
Scoring notes: Reverse-score: 7, 11, 14, 21, 25

Total Difficulties: Sum all except 1, 4, 9, 17, 20
Emotional Symptoms: 3, 8, 13, 16, 24
Conduct Problems: 5, 7, 12*, 18, 22
Hyperactivity: 2, 10, 15, 21, 25
Peer Problems: 6*, 11, 14, 19, 23
Prosocial: 1, 4, 9, 17, 20

* = our items slightly differ from the original/established measure.

Source: Goodman, R. (1997). The Strengths and Difficulties Questionnaire: A research note. *Journal of Child Psychology and Psychiatry, 38*(5), 581-586.

SDQ

Instructions

For each item, please mark the box for **Not True, Somewhat True or Certainly True**. It would help us if you answered all items as best you can even if you are not absolutely certain. Please give your answers on the basis of how things have been for you over the last six months.

	Not True	Somewhat True	Certainly True
1. I try to be nice to other people. I care about their feelings	□	□	□
2. I am restless, I cannot stay still for long	□	□	□
3. I get a lot of headaches, stomach-aches or sickness	□	□	□
4. I usually share with others, for example CD's, games, food	□	□	□
5. I get very angry and often lose my temper	□	□	□

6. I would rather be alone than with people of my age □ □ □

7. I usually do as I am told □ □ □

8. I worry a lot □ □ □

9. I am helpful if someone is hurt, upset or feeling ill □ □ □

10. I am constantly fidgeting or squirming □ □ □

11. I have one good friend or more □ □ □

12. I fight a lot. I can make other people do what I want □ □ □

13. I am often unhappy, depressed or tearful □ □ □

14. Other people my age generally like me □ □ □

15. I am easily distracted, I find it difficult to concentrate □ □ □

16. I am nervous in new situations. I easily lose confidence □ □ □

17. I am kind to younger children □ □ □

18. I am often accused of lying or cheating □ □ □

19. Other children or young people pick on me or bully me □ □ □

20. I often offer to help others (parents, teachers, children) □ □ □

21. I think before I do things □ □ □

22. I take things that are not mine from home, school or elsewhere □ □ □

23. I get along better with adults than with people my own age □ □ □

24. I have many fears, I am easily scared □ □ □

25. I finish the work I'm doing. My attention is good □ □ □

Supplement C8

Questionnaire Used to Assess Post-Cyberball Task Experience

Social Judgment Task Experience

Purpose: Assess perceptions after Cyberball.
Reporter: Adolescent self-report
No. of items: 9
Data collection: Time 1

Cyberball Task – SJTE

Please indicate your experiences during the social judgment task that you just completed.

1 What percentage of throws was directed at you?
2 Indicate percent of throws you were included.
3 Indicate percent of throws you were excluded.

		1 Not at all	2	3 Moderately	4	5 Very much so
4	I was included.	1	2	3	4	5
5	I was excluded.	1	2	3	4	5
6	I feel bad.	1	2	3	4	5
7	I feel sad.	1	2	3	4	5
8	I feel friendly.	1	2	3	4	5
9	I feel relaxed.	1	2	3	4	5

Supplement C9

Questionnaire Used to Assess Post-Cyberball Need Threat

NTS (Need-Threat Scale)

Purpose: Assess need threat after Cyberball.
Reporter: Adolescent self-report
No. of items: 12
Data collection: Time 1
Variables: C03SJTNTS01 – C03SJTNTS12; T2_C03NTS01 – T2_C03NTS12
Coding: 1 = Not at all, 3 = Moderately, 5 = Very much so
Scoring: See syntax file.
Scoring notes: See syntax file.
Source:

Cyberball Task – NTS

Please indicate the extent to which you felt the following feelings during the social judgment task that you just completed.

		1 Not at all	2	3 Moderately	4	5 Very much so
1	I felt "disconnected."	1	2	3	4	5
2	I felt rejected.	1	2	3	4	5
3	I felt like an outsider.	1	2	3	4	5
4	I felt good about myself.	1	2	3	4	5
5	My self-esteem was high.	1	2	3	4	5
6	I felt liked.	1	2	3	4	5
7	I felt invisible.	1	2	3	4	5
8	I felt meaningless.	1	2	3	4	5
9	I felt non-existent.	1	2	3	4	5
10	I felt powerful.	1	2	3	4	5
11	I felt I had control over the course of the task.	1	2	3	4	5
12	I felt superior.	1	2	3	4	5